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PANEL DISCUSSION ON CARDIAC AND CIRCULATORY DISEASES*

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MODERATOR STONE: It is unnecessary to emphasize the importance of cardiac and circulatory diseases in the geriatric age group. As the life span of our population continues to increase, these disorders will continue unless improved measures are developed for their prevention. The manifold problems in this regard beset all of our people in general, and the medical profession in particular.

This panel will discuss a variety of situations in the over-all group of cardiovascular diseases, particularly as they affect older persons.

The panel desires wide audience participation, and cordially invites you to present written questions that will be taken up at the end of the discussion.

First, I shall ask Dr. Griffith to discuss what can be done to delay the onset of degenerative cardiovascular diseases in professional and executive people after the age of 50 years.

DR. GRIFFITH: By your presence here, I know that you are greatly concerned, as I am, about the problem of the executive and the professional man. Physicians die at an average age of 55 years. The average executive dies at the age of 61 years. If you want to live long, you ought to be a minister. In this country, they live to 81 years of age.

I have been much concerned about the attitude prevalent even among physicians that after 50 years of age—or even as early as 40 years—the die is cast and little can be done to add either length or enjoyment to life. Too often, physicians themselves fail to take advantage of the help that medicine has to offer, as was brought out forcibly some years ago at the annual meeting of the Class of

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1900 of Columbia University Medical School. Until that time, an increasing number of class members died in each succeeding year, but following careful health surveys of the individual members and recommendations by the Committee on Longevity appointed at that meeting, both mortality and morbidity dropped significantly. Although 7 members died in the year before the committee went into action, in the second year of the program, the number of deaths among class members dropped to 5 (the average for persons in this age group); in the third year, there were 2 deaths; and in the fourth year, only 1 death. Even more noteworthy were the gains in active and creative enjoyment of life.

Programs of other groups, such as the United States Rubber Company, also have demonstrated that preventive measures will cut mortality and morbidity rates significantly among persons in the middle years and beyond. At the time of their initial survey in 1949, 1 executive in 5 was overweight, 1 in 6 had heart disease, and 1 in 7 had elevated blood pressure. Five years later (the end of 1954), after corrective measures had been taken, abnormal weights had been reduced so that only 1 in 15 of the executives was overweight. The incidence of hypertension had been reduced by half, and demonstrable heart disease had decreased by 48 per cent.

The program of the General Petroleum Company for its executives has had similar results. This program, which includes female as well as male executives and incorporates a study of serious gastro-intestinal diseases, has reduced the incidence of executive failure by more than 50 per cent.

In these companies, as in others with similar programs for employees and executives, general health measures come under consideration first. If a man is overweight, he is expected to reduce his weight to approximately 10 per cent more than he weighed at 21 to 25 years of age. Second, a careful health survey is made and correctable diseases treated. Third, an attempt is made to reduce the number of misfits among the executives. At the time a man is considered for upgrading, they consider his physical and his mental qualifications for the job. If he proves unsuitable for mental or physical reasons, he either is not promoted or he is transferred to a job for which his capabilities fit him—perhaps one which requires less responsibility.

Investigations have disclosed that the average executive, instead of working forty hours a week as does the day laborer, takes his work home with him. In addition, he entertains clients one or two nights a week. As a result, he works not forty but an average of forty-eight to fifty-four hours a week in order to hold his job. The correction of factors such as these is of great importance.

Also of importance is educating persons to exercise regularly by walking, swimming, or some other type of exercise suited to their emotional and physical needs. It is not healthful to become a week-end athlete, or to work hard all day and then rush out to the golf course for a brisk workout for an hour or two before dinner.

Thus, you see that both members of our profession and executives over the age of 50 years can do much to cut morbidity and mortality rates.

MODERATOR STONE: Dr. Montgomery, how would you evaluate the competency of the peripheral circulation?

DR. MONTGOMERY: For this discussion, I shall divide the peripheral circulation into arterial and venous components and omit the latter. We are talking about persons in the older age group, in whom the arterial problem is usually the more important.

Even before symptoms appear, the fact that a patient is in the geriatric age group should indicate to the physician a responsibility to seek in the history and physical examination early symptoms or signs of peripheral arterial disease.

There may well be minor or major symptoms. One, perhaps as common as any at the onset, is some degree of intermittent claudication. The history must be accurately taken, because it can be deceptive if the observation is not made that the pain comes on after a certain distance is traveled and is promptly relieved or greatly decreased just after the exercise stops.

Abnormal coldness of one extremity is suggestive, especially if it is more pronounced than in the contralateral limb. It is well to remember, however, that one extremity being colder than the other does not prove the existence of peripheral arterial occlusion or spasm in the cooler limb. Sometimes the warm foot is warm by reason of a low-grade infection, such as simple dermatophytosis, and the cool foot has normal vasomotor tone with no inflammation and no arterial disease.

More severe symptoms are immediately recognizable, such as severe intermittent claudication, pain in a foot at night, and lesions that do not heal.

I should like to emphasize a few points about the physical examination. In the elderly, it is important, even in the absence of symptoms, to make sure that the patient has all of his peripheral pulses. If he does not, one should attempt to determine whether or not the absence of a pulse or pair of pulses (such as the dorsalis pedis) is due to an anomaly rather than to occlusion. An anomaly accounts for 2 to 5 per cent of the cases.

A quick way to recognize fairly severe grades of arterial occlusion is to notice the blanching that characteristically occurs when a foot with poor arterial supply is elevated. On lowering the foot to a dependent position, both return of color and venous filling are usually slow. Toward the end of the test, when the foot is down, the development of a deep cherry red color is a bad sign, the "rubor of dependence" denoting severe ischemia.

Many physicians do not take the peripheral pulses routinely in patients having no obvious symptoms. Because of this lack of practice, they are unable to find the pulses quickly and to judge with assurance whether the pulses are normal or abnormal. There are two or three tricks, as most of you know. By and large, a femoral pulse is felt best by all of the fingers of the hand held flatly high over the femoral triangle (Fig. 1, No. 11), not by a single poking finger-tip. A popliteal pulse is felt best by both hands, with considerable controlled pressure (Fig. 1, No. 10).

In palpating the pulses of the lower extremities, it is advisable to have the

patient in a supine position. The examiner should sit when palpating the ankle pulses and stand when palpating the other pulses. Efficient positions for the examiner's hands, in relation to the patient's pulses, are shown in Figure 1.

Capillary pulsations in the examiner's fingers may be mistaken for a pulse of the patient. Thus it is important to time a doubtful pulse with, say, the patient's radial pulse. Fat and edema can make even a normal pulse difficult to feel. An oscillometer may than be helpful.

Figure 2 shows an experimentally demonstrated relationship between skin temperature at a constant room temperature (here 20° C. (68° F.)) and actual blood flow in the toes. In a patient who has lost pulses, you may suspect that there is a decreased blood flow in the foot, but you do not know to what extent it is decreased. If a simple so-called vasodilatation test is performed, that is, if the patient is thoroughly warmed in a constant-temperature room, or the sympathetic innervation is interrupted by an injection of procaine, the temperature of the normal toe rises according to the curve shown in Figure 2. In proportion as the blood flow is curtailed by an organic obstruction, the rise in skin temperature in this curve is limited.

I have seen patients lose three or four pulses and still retain such good collateral circulation in the foot that the curve approached normal. When this happens, it gives great assurance in the handling of elderly patients.

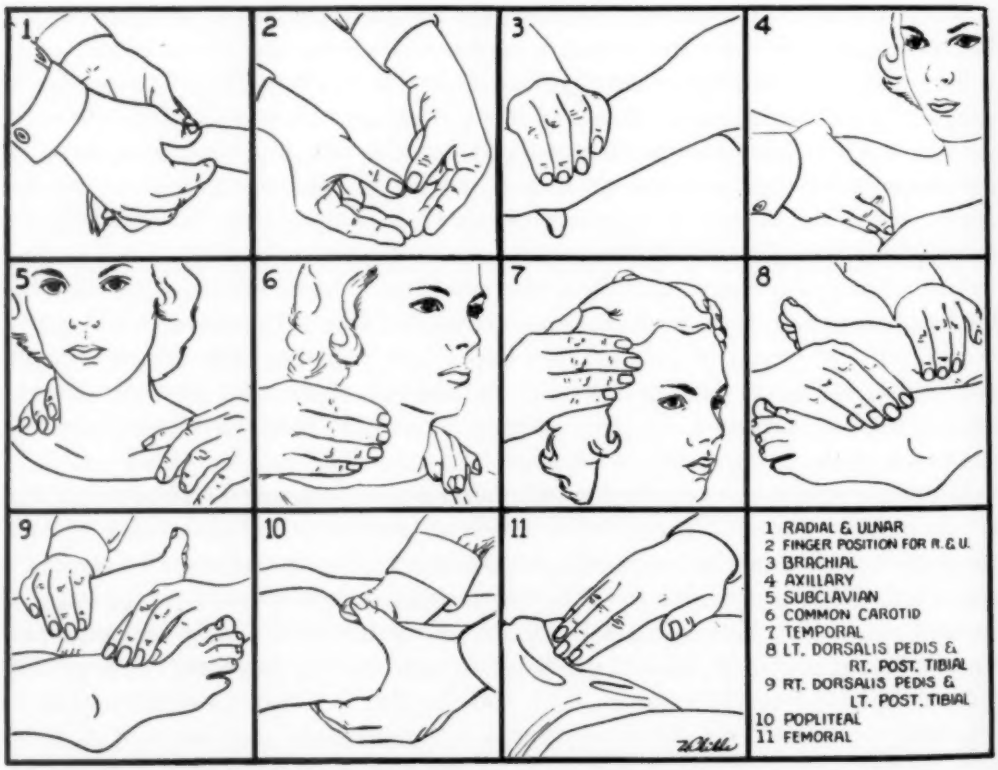


FIG. 1. Taking of the common pulses. (Reproduced with permission from Montgomery, H.: Pulses in arterial disease. Cardiovascular Brief, *Pennsylvania M. J.* **57:** 59, 1954.)

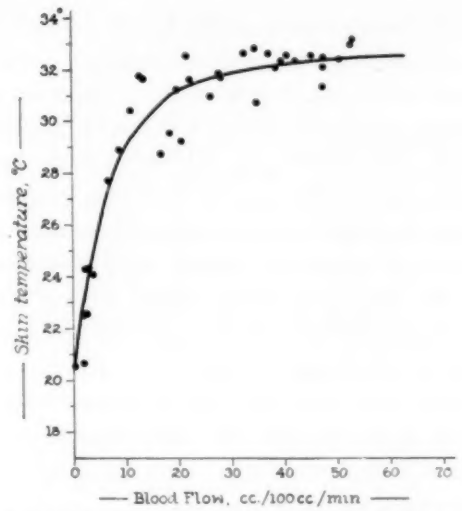


FIG. 2. Relationship of skin temperature of the toe to blood flow in the toe. Blood flow measured by venous pressure plethysmograph. (Reproduced with permission from Felder, D.; Russ, E.; Montgomery, H., and Horwitz, O.: Relationship in the toe of skin surface temperature to mean blood flow measured with a plethysmograph, *Clin. Sc.* **13:** 251, 1954.)

MODERATOR STONE: Before we proceed, we should orient ourselves as to the type of cardiac disease we expect to find in older people.

Dr. Paul, will you discuss that for us?

DR. PAUL: The obvious answer would seem to be that most older patients with cardiac disease have either coronary heart disease or hypertensive heart disease, or a combination thereof.

This generalization is not entirely true. As a result of the widespread impression that most people in this age group die as a result of one of these conditions, we often overlook other diseases which are somewhat subtle in their manifestation but which require attention and treatment if the patient's life is to be saved.

Arteriosclerotic heart disease is entered on many death certificates and on many hospital certificates. At the necropsy table, the diagnosis is frequently proved to be incorrect. Any hospital with a good pathological service will supply information at the end of each year revealing that several such diagnoses were in error.

Therefore, before we assume that all, or most, older people dying with heart disease die as a result of one or both of these common conditions, we should review the other kinds of heart disease that occur in older persons.

I grant that arteriosclerosis of the coronary artery prevails to some extent in almost all of us; and in the older age group, coronary occlusions and thromboses are widespread and important problems. The same is true of hypertension, although it is difficult in many instances to determine to what degree hypertension contributes to the death of the patient. Do the signs of a mild degree of hypertension found at the patient's death indicate that hypertension was the cause of death, or was death due solely to associated coronary disease? We know, for example, that patients with coronary heart disease or coronary arterio-

sclerosis may have some enlargement of the heart, so the relative importance of these two conditions is sometimes difficult to judge.

Conditions frequently overlooked and often present in the older patient are: 1) valvular heart disease, particularly aortic stenosis; 2) acute cor pulmonale due to pulmonary embolism and infarction, which in turn aggravates or produces congestive heart failure and death; and 3) bacterial endocarditis.

I have been humbled this past year by cases of disease in the older age group that have been difficult to diagnose during life, but have yielded somewhat surprising findings at the necropsy table. There is ample evidence in the literature to show that the diagnosis has been incorrect in most older patients dying with bacterial infection in the heart valves.

Although hypertension and coronary heart disease are the most important types of cardiac disease, a significant and important group of patients (some of whom have treatable disease) are dying from pulmonary embolism, bacterial endocarditis, or unsuspected valvular disease.

DR. GRIFFITH: How often do you encounter hyperthyroid disease and pericardial friction rub in the older age group?

DR. PAUL: Hyperthyroidism also is often missed in the older age group. Any patient with heart disease of obscure origin, particularly in the presence of auricular fibrillation, should be studied for thyroid disease by determining the basal metabolic rate and, if possible, the serum protein-bound iodine level.

The presence of a pericardial friction rub, which may produce pain simulating that in myocardial infarction, is important in the differential diagnosis of that condition. A pericardial friction rub may indicate uremic pericarditis, metastatic cancer of the pericardium, or a bacterial infection of the pericardial cavity. It may, of course, occur with myocardial infarction itself.

Acute, benign, idiopathic pericarditis is not often seen in the older age group, although it does occur.

MODERATOR STONE: Dr. Pratt, will you discuss the conservative treatment of occlusive arterial disease?

DR. PRATT: That also is a large assignment.

The treatment of occlusive arterial disease varies from sending a patient to a spa or some warm place until his money is exhausted, to covering the foot with sugar, a practice which—believe it or not—I have seen within the last week.

We recently carried out some research on 536 people who were over 40 years of age, not disabled, and working. Table 1 shows the extremely high incidence of

TABLE 1

Incidence of Calcification by Severity between the Sexes

	Total No.	No. with Calcification	No. with 3+ and 4+ Calcification
Men	305	135 (44%)	41 (30%)
Women	231	42 (18%)	3 (12%)

(Reproduced with permission from Lake, M.; Pratt, G. H., and Wright, I. S.: Arteriosclerosis and varicose veins; occupational activities and other factors, *J.A.M.A.* **119:** 696, 1942.)

TABLE 2

Prophylactic Treatment of Occlusive Arterial Disease

1. *Elimination of vasoconstriction*
   - Physical, *e.g.*, garters, casts, tourniquets, etc.
   - Drugs—ergot, adrenaline
   - Smoking!!
2. *Prevention of breaks in the skin and infections*
   - Hygiene
   - Foot care
   - Avoidance of extreme cold or heat
   - Trauma
3. *Stimulation of collateral circulation*
   - Medical measures
     - Walking, short of fatigue
     - Soaks and baths; swimming in moderation
     - Postural changes
     - Drugs
   - Anticoagulant drugs
   - Interruption of sympathetic nerves
     - Local blocks
     - Chemical
     - Surgical

calcification found roentgenographically, and the sex difference in incidence. The sex variation applies to the severe or plaque-like deposits of calcium as well.

We are not able to explain the sex difference; we used to try to blame it on the fact that the male smoked or drank or did other injurious things, but now the female does them to the same or to a greater degree.

In summarizing treatment I shall not go into details about any of the medicinal therapy, because other panelists are more capable than I in that sphere. Three basic points should be the foundation for treatment of these conditions: 1) elimination of constriction, 2) avoidance of injury to the part, and 3) stimulation of collateral circulation (Table 2).

Primarily, one should eliminate all sources of vasoconstriction, whether physical or medical. We have developed strong opinions as to the adverse effect of smoking on diseased vessels. As this is a lengthy subject, I shall say no more about it at this time.

The second point in therapy is the attempt to keep the covering, or envelope, of the extremity intact. This means not only keeping it intact, but also preventing infection. Breaks in the skin, due to carelessness or injury, may precipitate the change that often results in amputation. Most of the patients who undergo amputation recall having burned or traumatized themselves to a mild degree. The foot with normal circulation would promptly heal, but in these subjects a chain of pathologic events is set up that often terminates in amputation.

Proper care of the feet is important. We spend a great deal of time training the patient in hygiene of the feet. No one's feet are clean, but if they are not kept clean, and a skin break occurs, infection (which is usually the decisive factor) will be introduced. We tell our patients to wash their feet many more times a day

than they would their faces, and to use white cotton stockings so that soiling may be readily detected.

Extreme changes of hot and cold should be avoided. Many patients have difficulty with the circulation immediately after a severe sunburn, chilling, or wetting of the feet.

Every effort should be made to prevent trauma, whether at work or around the home or yard, with a view to keeping the skin intact.

When we come to the third point in conservative treatment, we are singing in the air to some extent. I am not sure any of us can stimulate collateral circulation. Use of the part up to the point of fatigue has seemed an ideal way. We tell patients to walk, but if they find that after three blocks they are tired, they are to stop at two blocks. We also initiate postural changes by raising and lowering the legs many times a day. Warm baths help the circulation, and swimming below the fatigue stage is advocated.

We feel certain that, when the laboratory problems involved in long-range antithrombotic control are solved, anticoagulant drugs will become part and parcel of the treatment of all of these patients. The final pathologic episode that ends in gangrene is always a clot, and in the patient who has occlusive disease the tendency to clotting is already in his blood. Clot formation occurs more readily under conditions of trauma and cold. The tendency can be reduced by use of anticoagulant drugs.

Another important point in the management of occlusive arterial disease is the interruption of the sympathetic nervous system, which will be discussed later.

MODERATOR STONE: We all have problems in connection with maintaining a normal fluid and electrolyte balance in patients with cardiac disease, chiefly in those with congestive heart failure.

Dr. Fox, will you discuss the changes that take place in fluid and electrolyte balance at the onset of congestive heart failure?

DR. FOX: Not a great deal is known about this topic. Only in recent years have most of the hospitals caring for cardiac patients been equipped with flame photometers which permit frequent analyses for sodium and potassium in the study of these balances.

Some years age, Dr. A. G. White, Dr. C. Friedberg, and I studied a group of patients admitted to Mt. Sinai Hospital because of congestive heart failure. We were surprised to find that most of them had rather marked abnormalities in the electrolyte pattern on admission.

Figure 3 summarizes some of our findings. It may be seen that none, or almost none, of the patients had normal values for serum sodium and chloride concentration on admission.

Some of the values for chloride were high and some were low. Prior to the days of flame photometry, this variation was one of the things that misled investigators who were making chloride measurements.

Some of the values for serum sodium were extremely low, but in an occasional patient there was a high concentration on admission.

It might appear that the low values were the result of salt restriction and ex-

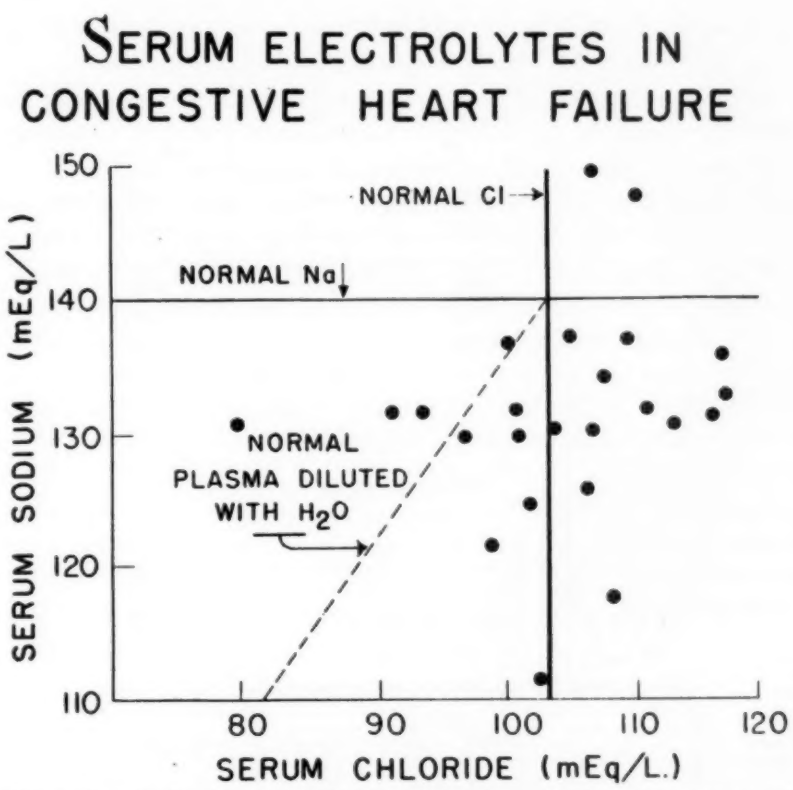


FIG. 3. Serum levels of sodium and chloride at the time of admission, compared with the average normal values represented by the horizontal and vertical lines, respectively. Sera with normal values for both Na^+ and Cl^- would be plotted at the intersection of these lines.

cessive water intake. However, the broken line in Figure 3 represents the concentrations that would have been obtained if water had been added to the patients' serum. Few of the actual values fell in that range. It is important to recognize that in congestive heart failure there may be a variety of alterations from normal in serum sodium and chloride levels, and that these are not merely the result of dilution.

Bicarbonate levels are not shown in Figure 3, but they too were abnormal—some were elevated, and some were low.

The serum potassium levels were also of interest. In general, unless the patient was anuric, the potassium level was low.

These values take on added significance when one starts to treat the patient. As the patient improves, the values return toward normal. Those that are above normal decrease, and those that are subnormal increase.

In Table 3 is shown an example of the action of a mercurial diuretic on sodium and potassium excretion. The patient received an injection of Mercuhydrin on the first, fifth, thirteenth, and seventeenth days of the study. His weight, which was 84 Kg. at the beginning, ultimately decreased to 69 Kg. The urinary volume was large at first. After the first injection, the excretion of potassium was high—

TABLE 3

Excretion of Electrolytes During Repeated Mercurial Diuresis

Day of Injection	Body Wt. (Kg.)	Vol. of Urine (cc.)	K^+ Total mEq.	Na^+	
				mEq./liter	Total mEq.
1	84	3800	145	76	290
	—	4100	121	63	260
5	79	3500	105	110	390
13	73	3700	74	139	518
17	69	1700	56	133	226

(Chlorides equal or exceed Na^+)

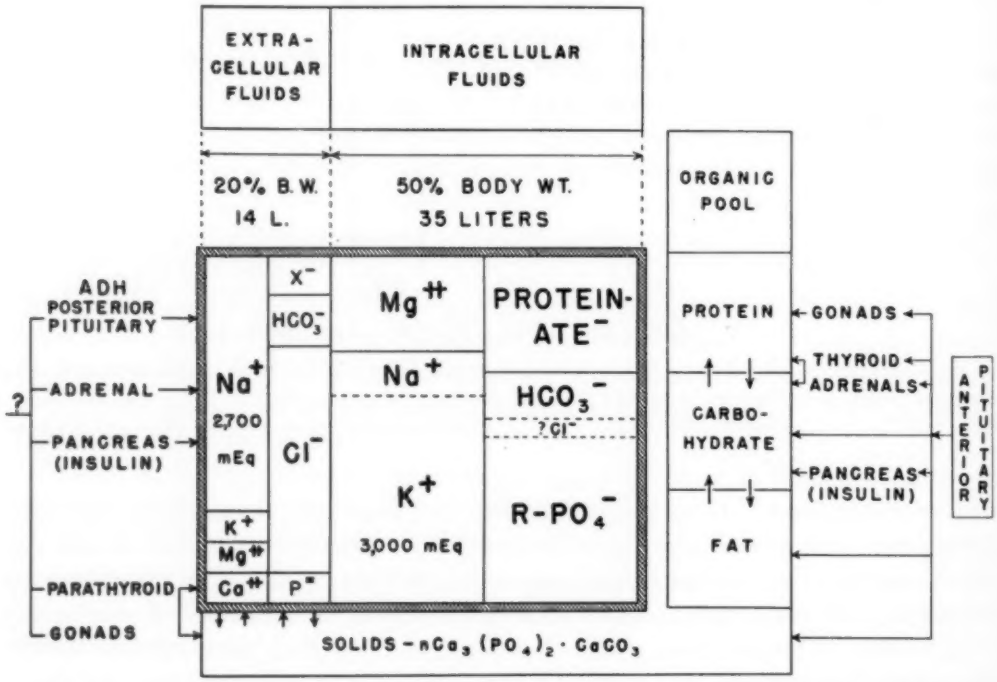


FIG. 4. Interrelationships of electrolytes and endocrines in man—a coordinated heterogeneous system. Horizontal axis indicates total volume in liters; vertical axis indicates concentration in mEq./liter, the total height representing 155 mEq./liter. The figure is drawn to scale, so that the area for each component represents the approximate total quantity in the body. (Modified from Hastings, A. B. *in* Report of 3rd M & R Pediatric Research Conference on Carbohydrate Metabolism, 1952, auspices of Ross Laboratories, Columbus, Ohio.) (Reproduced, with permission, from Fox, C. L., and Lasker, S. E.: Fluid therapy in surgical emergencies including hemorrhages, loss of gastro-intestinal fluids, and thermal burns, *S. Clin. North America* **35:** 335, 1955).

145 mEq. and 121 mEq., a total of 266 mEq., which is approximately the quantity of potassium a person normally excretes during four or five days when eating meat every day. Later in the study the urinary potassium loss decreased.

Conversely, although the patient lost a large quantity of sodium in the begin-

ning, proportionately more water was lost. Thus, sodium levels in the urine were extremely low. Had the urine been like edema fluid, the level would have been about 140 mEq. per liter, but it was only 76 mEq. Later, the urine became almost isotonic.

The early tendency, therefore, is to lose water, potassium and sodium. Later on, less potassium but more sodium than water is excreted. These data have significance which extends beyond their immediate visualization.

Figure 4 illustrates the composition of the body. The potassium concentration in the cells is about the same as the sodium concentration outside the cells. This means that the osmotic pressures of both compartments are similar.

Figure 5 indicates what happens when the plasma sodium level is lowered, as occurs in some patients with congestive heart failure. Normal relations are shown in the center. The size of the cells in relation to a normal plasma sodium level is illustrated. If the sodium level falls, as shown on the left in Figure 5, water must enter the cells, and they become enlarged. In contrast, if the sodium level rises above normal, water is drawn out and the cells become shrunken or dehydrated, as shown at the right. When the plasma sodium level falls, some potassium may leave the cell. This happens frequently when a mercurial diuretic is given.

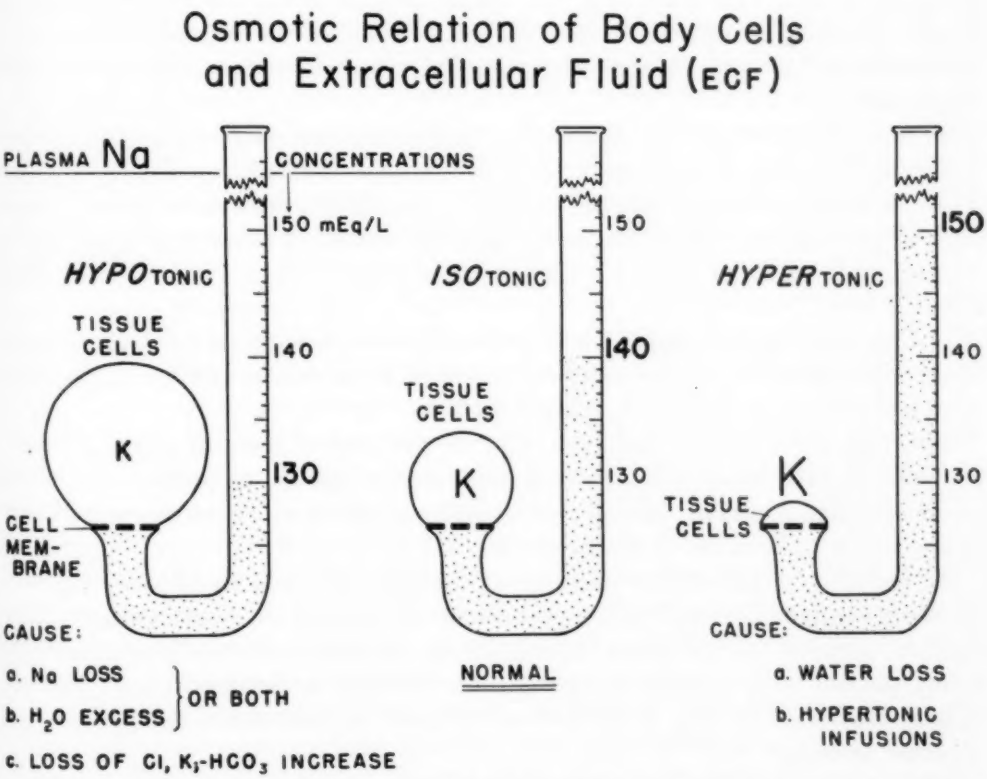


FIG. 5. Changes in electrolyte pattern under conditions of lowered plasma sodium level, as in some patients with congestive heart failure, illustrating size of cells in relation to normal sodium level (center); low and high values are on left and right respectively.

Thus, we see that the pattern of electrolytic alterations in congestive heart failure is most complex. There are changes not only in the extracellular fluid and in the plasma, but also in the cells of the body. I need not remind you that one of the important groups of cells is the myocardium. These alterations in the cells may be an integral part of the disturbance that we recognize as heart failure.

MODERATOR STONE: Now that we have established a base line, so to speak, I shall call on Dr. Griffith to discuss the common complications of myocardial infarction.

DR. GRIFFITH: Los Angeles is often referred to as the "City of the Living Dead." This is particularly true of my section, around Pasadena. In the Los Angeles County Hospital, we have averaged 1,117 myocardial infarctions per year during the last five years. It behooves us to see what can be done about the situation. One does not die from myocardial infarction itself, but from the complications induced by it.

We have examined the necropsy records of 1,000 patients with myocardial infarction. Patients in certain wards were treated prophylactically with anticoagulants. Those in other wards were treated in a more conservative manner.

Thirty-seven per cent of the patients not treated with anticoagulants had thrombo-embolic manifestations. We firmly believe in the use of anticoagulant drugs. Necropsy records show that only 4 per cent of the treated patients had demonstrable thrombo-embolic manifestations, such as venous thrombosis with pulmonary embolism.

Twenty-two per cent of the patients in both series had congestive heart failure.

Twenty per cent of the patients went into a state of shock. By shock, we mean a serious drop in blood pressure to below 80 mm. Hg in a previously normotensive individual, with the pressure remaining at the low level unless the hypotension was treated, accompanied by other manifestations such as vomiting and cold, clammy skin.

Serious arrhythmia occurred in 17 per cent of the patients, as determined from electrocardiographic records or from the charts. By serious arrhythmia, we mean ventricular tachycardia, or fibrillation, or both.

Although it may seem incredible, fully 10 per cent of the patients in the necropsy series were found to have myocardial aneurysms. In our series, none of the aneurysms had ruptured. Rather, the aneurysms had resulted in congestive heart failure due to dilatation of the ventricle.

Six per cent of the patients had ruptured hearts, that is, a small area of necrosis went straight through the myocardium. In almost all these subjects, the rupture occurred at the point where the ventricular wall meets the septum. Every patient with a ruptured myocardium had had a sustained blood pressure of more than 200 mm. Hg. In the light of the latter finding, the mode of treatment is rather obvious.

The next two complications were gleaned from the charts and from the clinic records. In 15 per cent of the patients the shoulder-hand syndrome developed. Perhaps Dr. Montgomery and Dr. Pratt will tell us how to prevent this.

I do not know what to do about the last finding. We noted that, after even a minor cardiac infarction, cardiac neurosis developed in up to 85 per cent of patients. We, as physicians, must accept the blame for this.

MODERATOR STONE: Dr. Paul, you mentioned the importance of aortic stenosis.

DR. PAUL: First, I should like to make an addition to Dr. Griffith's remarks. He mentioned the fact that in his series of myocardial aneurysms there were no ruptures. When I took my special examinations in cardiology some years ago, I gave that answer essentially as he has given it to us, and the pathologist who examined me promptly produced two specimens in which the aneurysm had ruptured. The pathologist was Dr. Edwin Hirsch, who is a very capable person. Rupture is a rarity, but it does occur.

With reference to aortic stenosis, the symptoms are often missed in the older age group, and the physical findings accompanying it are often overlooked. A patient in whom pulmonary edema suddenly develops, or a patient who has episodes of faintness or dizziness, should be particularly investigated with the thought that he or she may have a calcifying aortic stenosis.

If the patient has chest pain that is not quite like the usual angina pectoris and is longer in duration than angina caused by coronary arteriosclerosis, aortic stenosis may be the cause.

The detection of aortic stenosis by physical examination is often difficult. Contrary to classic textbook descriptions, in my experience the diagnosis is not necessarily dependent upon a combination of typical findings. Certainly in the typical case there is a rough aortic systolic murmur, the murmur is well transmitted to the apex of the neck, and there may be a thrill. Fluoroscopic examination may reveal calcification of the valve. The electrocardiogram shows left ventricular hypertrophy and the pulse pressure may be small. However, in many cases not all these findings are present.

Patients with aortic stenosis may have only a slight aortic murmur. Most of them do not have a thrill. Frequently, the pulse pressure is not narrow and many of the other signs are absent. Therefore, the diagnosis must be suspected on the basis of some of the symptoms I mentioned.

Aortic stenosis should be particularly suspected in a patient who has a rough, whiny, or seagull-cry systolic murmur in the aortic area (often well heard at the apex), regardless of its intensity and essentially regardless of whether or not calcification is visible fluoroscopically in the aortic valve.

Many people in the older age group die from aortic stenosis, and those acquainted with coroners' statistics know that not uncommonly a coroner may find that aortic stenosis was the cause of sudden death in a patient not previously known to have heart disease.

Aortic stenosis is a serious, formidable condition. Once the symptoms appear, the patient runs a rapid downhill course. Treatment is not satisfactory.

DR. GRIFFITH: For patients in the older age group, are you recommending Bailey's operation—entering through the aorta and dilating the stenotic aortic valves—or are you recommending the new bypass method, with a plastic tube?

DR. PAUL: I am extremely pessimistic about direct approaches on the aortic valve, whether they be through the ventricle or through the aorta. We have had experience with both types of surgery.

I am interested in your reactions. My opinion is that the likelihood of salvage is slight, and the mortality excessively high in the older age group. I would not recommend surgery.

I have had no experience with the bypass that interests Dr. Stanley Sarnoff.

MODERATOR STONE: Dr. Montgomery, what are the indications for sympathectomy when the blood flow to the limb is reduced?

DR. MONTGOMERY: I assume we are still talking about geriatric problems. It is unusual for a person of geriatric age to benefit from sympathectomy. The first criterion, which is almost always overlooked, is whether sympathectomy is really necessary; that is, whether the vasodilatation resulting from medical measures is incomplete. Excessive vasomotor tone associated with arteriosclerosis in older patients is usually wholly relieved by medical measures.

One should be able to demonstrate by the use of vasodilatation tests (described previously) whether any benefit is to be gained from sympathectomy. For instance, when dealing with decreased circulation in a toe or foot, it may be possible to demonstrate a considerable increase in blood flow through a procedure such as lumbar block. A significant increase would be a rise of at least several degrees Centigrade, because (as shown in Figure 2) such an increment is necessary to cause even a slight increment in actual blood flow when the initial temperature is near room temperature, as it is when there is severe ischemia.

If sympathectomy is considered in the treatment of intermittent claudication per se, a paravertebral block should be used first to demonstrate that this release of vasomotor tone does in fact result in considerable improvement in the patient's ability to walk. He should understand that he probably will derive no more benefit from a sympathectomy than he does from the paravertebral block.

In most patients, there is no indication that a sympathectomy will increase blood flow through muscle. There is every reason to believe that exercise increases this flow to the fullest possible extent. Only occasionally is a patient's walking improved by sympathectomy.

I hope Dr. Pratt will disagree with what I have said, to bring out the points under discussion.

MODERATOR STONE: I shall ask Dr. Pratt what his basis is, medically, for interruption of the sympathetic nervous system in arteriosclerosis.

DR. PRATT: As you know, we are all trying to rationalize our thinking about this subject. Our clinic has strongly advocated sympathectomy and has been somewhat out on a surgical limb in believing that surgical sympathectomy is nearly as important in the patient with occlusive arterial disease as appendectomy used to be in the disease known as "inflammation of the bowels" (appendicitis).

It will take some time for the center of the pendulum swing to be found. We are impressed every day not only with what can be accomplished in patients with occlusive arterial disease by sympathectomy, but also with what can be done for patients in the older age group.

During the last five years, we operated on 40 patients over the age of 85 years and lost 1 patient postoperatively, although a normal loss in that age group would be 2 deaths in the same length of time without any operation. As surgeons, we see these patients only after internists are through treating them. The patients do not elect surgery first, but only after every other method to gain relief has been tried. The fact that we have helped this "last hope" group is part of the reason why we are so pleased with results of sympathectomy.

I shall try to explain why sympathectomy actually works. The diagram in Figure 6 illustrates the old idea of vasospasm. The clot or the plaque initiates a reflex of either neurogenic or chemogenic type, causing spasm in the affected vessel and its collateral vessels, in the muscle as well as in the skin.

The final picture in any patient is the thrombus in the artery. Formation of this clot is often due to slowing of the blood stream. If the blood leaves the heart under normal systolic pressure (for example, 120 mm. Hg), by the time it has traveled the many miles of arteries and reached the end-arteries or arteriolar bed, the pressure has dropped approximately 30 points to 90 mm. Hg. By the time the blood passes through the capillary bed, the pressure has dropped to 30 mm. About 1,000 times as much pressure is used in transporting the blood through the capillary bed as in transporting it from the heart to the end-arteries.

We believe, and hope eventually to prove, that a reduction in this capillary

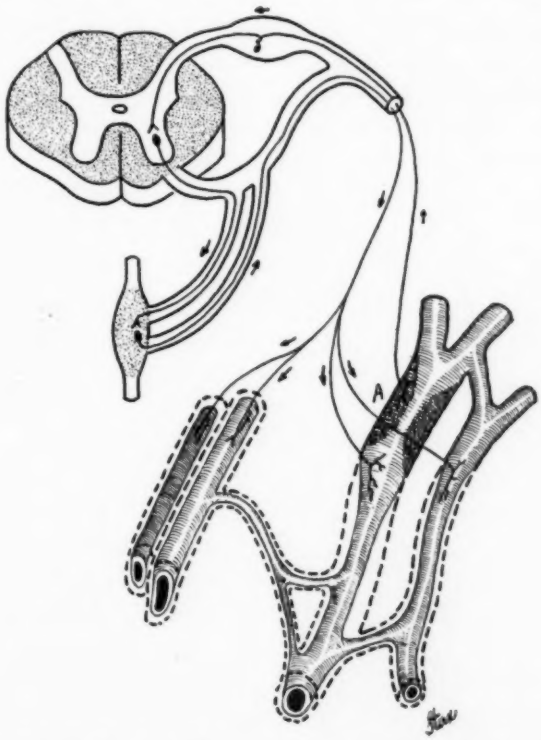


FIG. 6. Illustrating the mechanism of vasospasm in relation to the sympathetic nervous system. (Reproduced with permission from Pratt, G. H.: Cardiovascular Surgery. Philadelphia, Lea & Febiger, 1954.)

resistance, particularly in the arteriolar and capillary beds, accounts for the beneficial effect of sympathectomy.

Two things are important in considering the effect of sympathectomy upon the patient: 1) Will the patient survive the operation? 2) Will he have to lose his leg afterwards? In an attempt to answer these questions of such fundamental interest to patients, we reviewed a large series of surgical sympathectomies in patients from 17 to 87 years of age (Table 4). Since only 3 per cent died, the operation itself does not appear to be dangerous. This is proved also by the loss of only 1 patient among 40 who were over 80 years of age.

Following 309 lumbar sympathectomies, 62 amputations of the lower limb were performed, distributed by site as shown in Table 5. The infectious aspect of diabetes made a great deal of difference. Frostbite cases were included, but this should not have been done, as they were military casualties.

Table 6 shows the amputees' reasons for consulting a physician, before sympathectomy.

Amputation was performed in 4.5 per cent of patients with claudication in the older age group over a five-year period, and in 1 of every 3 patients in whom the skin broke and ulcerous infection developed. We find it necessary to perform amputations on 2 of every 3 patients with actual gangrene, but we still salvage 1 of these 3 patients. Pain at rest is not as much affected by sympathectomy as are the other symptoms.

It should be emphasized that the 4.5 per cent amputation rate (Table 6) refers to a group of 179 desperate patients with claudication who came either for amputation or for anything that we could offer, after everything else had failed.

TABLE 4

Postoperative Deaths among 309 Patients Undergoing Lumbar Sympathectomies for Occlusive Arterial Disease

Cause of Death	No. of Deaths
Coronary occlusion	5
Generalized arteriosclerosis	2
Progressive gangrene	1
Mesenteric thrombosis	1
Total	9
Mortality rate	3%

(Of the deaths, 7 occurred in patients over 60 years of age)

TABLE 5

Distribution of 62 Amputations Following 309 Lumbar Sympathectomies

	Number	Per Cent
Amputations of part of foot	3	5
Amputations below the knee	24	39
Amputations above the knee	35	56

TABLE 6

Amputation Rate after Sympathectomy in Relation to Symptoms

Symptomatology	No. of Sympathectomies	Amputations	
		No.	Per Cent
Coldness and claudication	179	8	4.5
Ulceration and infection	65	21	32.3
Gangrene	35	23	65.7
Pain at rest	16	8	50.0
Other symptoms	14	2	14.3
Totals	309	62	

DR. FOX: Figure 6, which indicates the pathways involved in this process, may be important. If we had more understanding of the functional disturbances, we might have better knowledge of what to do.

A curious recent occurrence illustrates this point. A child sustained a rather extensive burn, which involved the forearm and a little of the upper arm. About twenty-four hours later, the hand became cold. There was much discussion among the vascular surgeons and the plastic surgeons concerning whether or not to incise the burned areas in order to release the constriction which was presumably causing pressure on the artery and impairing the circulation. The vascular surgeons believed that the pressure was not sufficient to block the circulation. They believed the impairment of circulation was on a neurogenic or some other basis. The final decision was to make incisions to relieve the pressure. However, this procedure did not significantly alter the circulatory status.

We need to know more about what is actually happening, in order to decide whether or not to use a procedure such as sympathectomy to relieve any block which may be present.

MODERATOR STONE: You referred a short time ago to a large loss of potassium in patients with heart failure who were given mercurial diuretics. I should like you to tell us what effects potassium depletion has on heart failure.

DR. FOX: This is another problem about which we need more knowledge. An important question is, What does the serum potassium level tell about the status of cellular potassium?

Some patients with extremely low serum potassium levels have normal electrocardiograms. On the other hand, the electrocardiograms of some patients with normal serum potassium levels show marked abnormalities. Thus only certain patients with congestive heart failure, who have had numerous treatments with mercurial diuretics and have lost a great deal of potassium, will show disturbances in the electrocardiogram, although many may have low serum potassium levels. In contrast, patients who have sustained a loss of potassium and also have some degree of renal disease and associated electrolyte imbalances are more likely to show marked disturbances in the electrocardiogram.

There appears to be a fairly close relation between the effects of low potassium levels and toxic symptoms from digitalis. Potassium depletion and digitalis toxicity have certain electrocardiographic similarities.

The first vertical group of tracings in Figure 7 shows some of the more obvious changes in the electrocardiogram, almost characteristic of potassium deficiency. There is only a slight indication of a T wave, a suggestion of a U wave, and the QT interval is prolonged. Yet this patient's serum potassium level was normal—5.2 mEq. per liter.

Potassium was then administered. During therapy, the T wave became evident and the U wave disappeared. Subsequently, the patient was re-examined. The serum potassium level was only 1.8 mEq. per liter, but his electrocardiogram showed very little disturbance. Because of muscle weakness, he was given potassium therapeutically for a long time and the serum potassium rose to 3.0 mEq. per liter. One expects low serum potassium levels in association with electrocardiographic disturbances, but often they are normal.

Another situation is illustrated by the electrocardiogram in Figure 8. The patient, a child suspected of having Addison's disease and pseudohermaphrodism, received considerable saline therapy but no potassium. Nevertheless, there was electrocardiographic evidence of severe potassium toxicity. Four hours later, the electrocardiogram was normal. This is an example of potassium toxicity caused by adrenal hormonal deficiency inadequately treated.

To summarize some of these data—there may be a normal plasma level of potassium, with low bicarbonate, low chloride, and low sodium levels. There may be cellular potassium deficiency with disturbances in the electrocardiogram. A low chloride level may be associated with a high value for CO_2—the so-called potassium depletion syndrome with alkalosis. This is probably not an alkalosis like that observed after ingestion of sodium bicarbonate; although the serum potassium concentration would be normal, the cellular potassium and intracellular pH would be low. As electrocardiographic manifestations of potassium deficiency, the ST segment would be depressed, the QT interval lengthened, and the T wave depressed or inverted. The U wave is also a good indication of potassium deficiency.

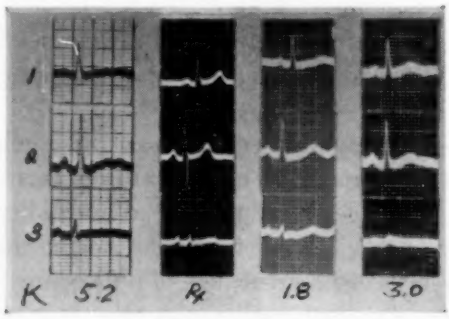
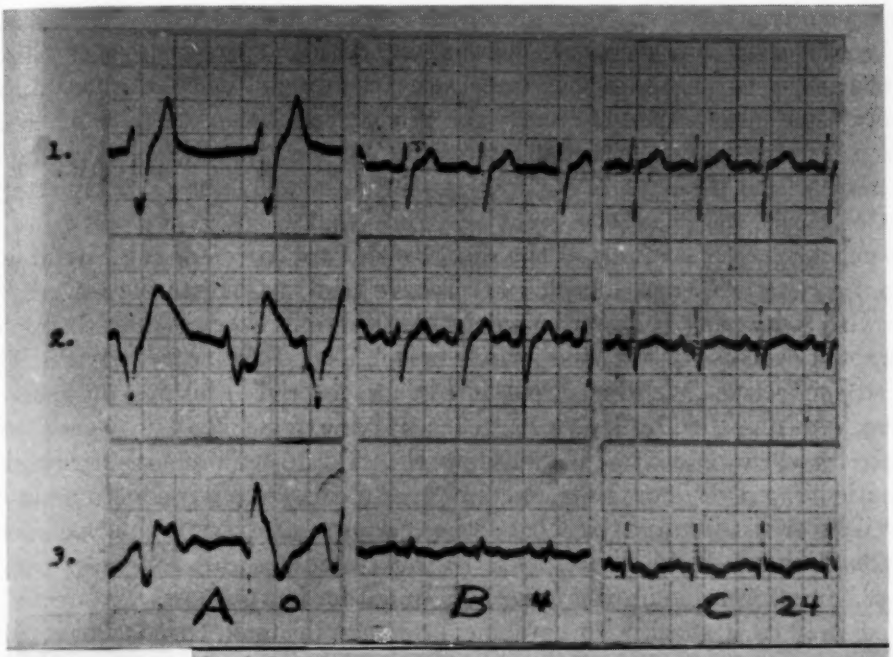


FIG. 7. Before treatment, the electrocardiographic changes were almost characteristic of potassium deficiency, yet the serum potassium level was normal (5.2 mEq. per liter). After treatment with potassium, the electrocardiogram showed little abnormality, although the serum potassium level was low (1.8 mEq. per liter) for a considerable period before rising to 3.0 mEq. (Reproduced with permission from Currens, J. H., and Crawford, J. D.: Electrocardiogram and disturbance of potassium metabolism, *New England J. Med.* **243:** 843, 1950.)



Serial Electrocardiograms Taken on Entry (A), Four Hours Later (B) and Twenty-Four Hours Later (C), Demonstrating a Marked Widening of the QRS Complexes, High T Waves and Absent P Waves, with an Idioventricular Rhythm Indicating Potassium Intoxication. In four hours the change is dramatic, with a relatively normal tracing although the QRS interval decreased further after twenty-four hours.

FIG. 8. Electrocardiograms in a child with Addison's disease and pseudohermaphrodism, in whom the adrenocortical deficiency had been inadequately treated, with saline but no potassium. On entry there was electrocardiographic evidence of potassium toxicity. Four hours later the electrocardiogram was normal. (Reproduced with permission from Currens, J. H., and Crawford, J. D.: Electrocardiogram and disturbance of potassium metabolism, *New England J. Med.* **243:** 843, 1950.)

In patients receiving maintenance digitalis therapy, it is interesting that intensive diuresis causing potassium loss may precipitate digitalis-induced arrhythmias. If a patient displays digitalis toxicity, it may be advisable to try administering potassium in the form of potassium acetate. Potassium depletion from any cause will enhance digitalis toxicity, and the administration of potassium salts will then relieve the toxicity.

MODERATOR STONE: Dr. Griffith, you mentioned that 20 per cent of your patients at the Los Angeles County Hospital who had myocardial infarction died of shock. Would you like to discuss this point?

DR. GRIFFITH: One can never tell whether or not a patient with acute myocardial infarction will slip into shock, either immediately or gradually. Roughly 20 per cent of our patients died of shock, so we thought that finding a solution to the problem was a real challenge.

We were convinced that the promptness with which antishock measures are employed is a factor in recovery. We were, at the same time, desirous of assessing the efficacy of various antishock measures. Accordingly, in 1951, we established a shock team and decided to treat vigorously and as soon as possible all cases of shock accompanying myocardial infarction. We were handicapped by the fact that most of our patients do not reach us until about five or six hours after the onset of shock.

In general, the first efforts of the shock team were centered on positioning the patient, giving sufficient morphine to relieve pain, administering oxygen, and otherwise controlling factors that might contribute to shock. When these measures were unsuccessful, we tried intravenous infusions of blood or plasma. These proved ineffective. We then tried retrograde arterial infusions, utilizing the method recommended by Irving Page. It was our experience that by the time we got the blood running into an arterial needle and into the brachial artery, either the patients were dead or the trauma involved in the process produced additional shock. We tried a number of short-acting vasopressor drugs with some success, but found that usually the response to these agents is lost relatively early in shock. Norepinephrine proved to be best suited for our purposes. At present, we immediately treat shock with norepinephrine administered by continuous intravenous drip at a rate adjusted to maintain blood pressure at the desired level.

In our experience, cortisone does not potentiate the effect of the vasopressor drugs. We have been unable to help patients in shock by any method other than the judicious use of norepinephrine. It is administered in a 5 per cent glucose solution through a long needle in the vein or, preferably, through a polyethylene tube. The solution is allowed to drip at a rate of not more than 10 drops per minute until the blood pressure response is determined. Then the dosage is increased to 8, 10, or 12 gamma of norepinephrine delivered to the blood stream per minute in order to keep the blood pressure at 110 or 120 mm. Hg, or wherever desired.

We found that sloughs occurred if the needle slipped out of the vein, or if the solution was allowed to run too rapidly. Sloughing also occurred if a thrombus formed in the vein, causing the solution to back up. About fourteen months ago we started putting 10 mg. of heparin into each 500 cc. of norepinephrine solution. Since then, we have had no more trouble with thrombosis and backing up of the fluid into the tissues.

The maintenance dosage of norepinephrine is administered until the patient is warm, dry, and out of shock, or for at least two hours. If the norepinephrine is discontinued abruptly, shock will recur; therefore, the drip rate is reduced by 1 drop per minute each hour.

The average length of time for giving norepinephrine is three hours. We have continued administration for as long as seven days, and had the patient live.

During an eighteen-month period between 1949 and 1951, before specific antishock measures were employed and before we had realized the importance of early treatment in combatting shock in these patients, 816 cases of unequivocal myocardial infarction were treated at the Los Angeles County Hospital. Among

these, there were 161 cases of shock that required vigorous treatment, and in this group there were 128 deaths—a mortality rate of 80 per cent.

In the eighteen months following the formation of our shock team, 134 patients were treated for shock accompanying myocardial infarction. We were able to institute antishock treatment in 60 patients within three hours after the onset of the shock syndrome. Of these 60 patients, only 13 per cent died—a survival rate of 87 per cent. By contrast, there was a survival rate of only 24 per cent among the 74 patients who received treatment more than three hours after onset.

Promptness of treatment and the early use of a vasopressor agent are most important in the treatment of shock.

MODERATOR STONE: In your judgment what blood pressure level is an indication for the use of norepinephrine?

DR. GRIFFITH: No matter what the heart rate or rhythm may be, when the pressure drops to 80 or below, and the patient has a cold, clammy skin and is nauseated, we start the administration of norepinephrine.

However, a person with myocardial infarction who has no drop in blood pressure, shows neither sympathetic nor parasympathetic reaction to the disturbance, and is not overactive, should not be given vasopressor drugs even though apparently in a shock-like state.

When shock occurs in patients with hypertension, we start treatment when the blood pressure is 100 to 110 mm. Hg.

DR. MONTGOMERY: I am interested in what Dr. Griffith said about the use of heparin with norepinephrine intravenously. Those who have used a considerable amount of norepinephrine for these purposes have occasionally encountered serious sloughing and vasomotor effects. I was not aware that the solution to the problem might be the prevention of clotting.

I should like to ask Dr. Griffith if he could give a rough estimate of how many patients in sequence were given heparin along with norepinephrine intravenously, without having significant local damage.

DR. GRIFFITH: We summarized the effects of treatment with norepinephrine only a month or so ago. Within the past fourteen months, we have treated 137 patients. No thrombosis occurred in any of the veins, and the only time we had difficulty was when the needle slipped out of the vein. When this happens, sloughing results whether heparin is used or not.

The idea of using heparin occurred to me when I was visiting Guyton at the University of Mississippi at Oxford. He put dogs into a state of shock. The shock was irreversible, and the dogs died after three hours. However, when he heparinized the dogs before hand, he was able to keep them in a state of shock for twelve hours, and the shock still was reversible. Sections of the brain and myocardium from dogs that had recovered showed no evidence of little capillary thromboses. To me, irreversible shock signifies the presence of thrombosis that destroys the heart and the brain.

DR. PAUL: My experience is similar to that of Dr. Griffith. Many physicians are reluctant to do what he has suggested because of fear that this is a dangerous drug and that perhaps they will complicate an already complicated situation.

I agree with Dr. Griffith that the administration of norepinephrine is a life-saving measure and should not be delayed.

Because of lack of time, he did not stress one factor, which I shall mention. When norepinephrine is given in excessive quantities, the blood pressure can rise to an extremely high level. The patients, therefore, must constantly be watched to insure that the level is maintained in the range that Dr. Griffith mentioned—somewhat over 100 mm. Hg systolic—rather than at a level of 150 to 200 mm. or more, which can be reached in a very few minutes if the drug is instilled too rapidly.

DR. GRIFFITH: Concerning the use of norepinephrine, I should like to say, first, that norepinephrine need be withheld from any patient because of advanced age.

Second, the arrhythmias that appear in association with myocardial infarction seem to be eliminated by norepinephrine as the blood pressure rises, and better perfusion of the coronary vessels results. At no time have we found the myocardium stimulated by the norepinephrine, as it would be by adrenaline.

When it is necessary to send the patient to the hospital, treatment is difficult. We advise our people, particularly those who accompany the patient in the ambulance, to give Vasoxyl every fifteen minutes while they are transporting the patient from his home to the hospital. This treatment will sustain the patient until he reaches the hospital and the administration of norepinephrine is begun.

However, an intravenous infusion can be given either in the home or in the hospital.

MODERATOR STONE: It is customary in many types of shock to give blood transfusions. Dr. Fox, have you had any special difficulties in giving blood transfusions when heart disease was present, either with or without myocardial infarction?

DR. FOX: I do not usually treat patients with heart failure; at present, my efforts are confined to the Department of Surgery. We have, however, made some studies of transfusion that may be of interest in connection with the problem of shock. It is fairly obvious that the patient who has had a myocardial infarct has not had loss of blood. Nevertheless, the circulation is in a bad state.

We should go back to the fundamental observations of Gamble and others on the nature of the circulation, in trying to understand what is happening. The blood itself is not in contact with the cells of the body, including those of the myocardium. All the substances that are brought to the cells are transported through the interstitial fluid. Oxygen leaves the blood and then moves through the interstitial fluid, in that way reaching the cell. Likewise, metabolites that leave the cell move through the interstitial fluid and then into the blood.

One might ask, as an experimentalist, whether or not it would be desirable to try to do something to improve the interstitial circulation in these patients.

They presumably have enough red cells; many of them have more than the normal amount. Theoretically, it might be of some value to improve the interstitial circulation by introducing material that resembles interstitial fluid. This

TABLE 7

Comparative Plasma (I^{131}-Albumin) and Red Cell Volumes (Cr^{51}): Effect of Single Blood Transfusion

Hematocrit (%)	I^{131}-Plasma Albumin		Cr^{51}-Red Cells	
	Plasma (cc.)	Blood (cc.)	RBC (cc.)	Blood (cc.)
Before, 40	3420	5710	1250	3120
*Transfusion of 625 cc. of Blood**				
After, 43	+370**	+970	+150	+120
Measured Blood Volume: 3420 + 1250 = 4670 cc.				

* One week after radical mastectomy—320 cc. cells and 305 cc. plasma.

** The post-transfusion values represent the change in each volume.

would not be sodium chloride alone, but a mixture of sodium chloride, sodium bicarbonate and some of the other salts that constitute interstitial fluid. It might be something like Ringer's lactate.

Table 7 indicates some of the things that happen when a transfusion is given. In the study, red cells were labeled with radioactive chromium and plasma albumin was labelled with radioactive iodine, so that these two components of the blood could be traced. The red cell mass and the plasma volume were measured before and after the transfusion of whole blood in a convalescing patient.

Although the patient was given about 320 cc. of cells and 305 cc. of plasma (total 625 cc.), her blood volume as determined by the I^{131}-albumin method increased by almost a liter. On the other hand, her blood volume as measured by the chromium-labeled red cells increased by only 150 cc. It would appear that a transfusion in some instances tends to expand the plasma volume enormously and scarcely increases the red cell volume.

Conceivably, in patients with heart failure, a transfusion might greatly expand the blood volume and only slightly expand the red cell volume, and this might not be desirable. Therefore, it might be worthwhile to study the effects of increasing the interstitial volume rather than the blood volume in patients with myocardial failure.

MODERATOR STONE: Our time is limited, and we must consider other subjects of great interest.

Dr. Montgomery, will you discuss the selection of patient for arteriography and aortography?

DR. MONTGOMERY: This is a new and exciting subject. It can be discussed with reference to the geriatric age group.

The patient in whom one uses an arterial graft is one who is threatened with a rupture of a great artery by reason of an aneurysm, or in whom a large artery is occluded. In this group of patients, pioneering surgery—replacing a dangerous bit of vessel with a presumably sounder piece of vessel—seems indicated. In peripheral vessels, there is still a question as to whether an homologous arterial graft or an autogenous vein graft should be used.

When the artery is occluded, there is the important question of whether a long segment or a short segment is occluded. Aortography and arteriography are of great help in this respect.

Dr. Pratt has much surgical experience in such cases, and I should like to hear his comments.

MODERATOR STONE: Dr. Pratt, will you discuss the surgical treatment of thoracic aneurysm of the aorta and of thrombosis of the bifurcation of the aorta?

DR. PRATT: The problem of occlusion of the major arteries has to be faced by all of us, because it is a life or death matter. The mere fact that patients are aged is not sufficient reason to bar them from the possibility of relief.

This work is still in the early stages, but the mortality is dropping. Until 1890, no patient had survived gastrectomy; and the mortality rate in 1900 for patients undergoing gastro-enterostomy was about 90 per cent. We are going to have a high mortality rate in the surgical treatment of aneurysms for a long time, because the vessels involved are poor and often will not hold sutures well.

A leaking aneurysm in either the thoracic or abdominal aorta poses a special problem, which can be solved surgically in some patients.

The removal of a diseased segment of an artery is not always indicated, even though desirable. That is easy to understand, when one realizes that removing the segment often simultaneously removes the collateral circulation, leaving no alternative pathways if the graft does not work. Therefore, in most instances we either disengage part of the artery and perform an end-to-end anastomosis, or perform a end-to-side anastomosis. If the patient does not improve, at least he is not made worse, other than having undergone an operation.

Examination of the vessels around the popliteal space in Figure 9 shows that there is not sufficient collateral circulation to carry the load. In a case of this kind, gangrene is nearly inevitable. The use of an homologous graft, or one of the new prosthetic devices, offers the solution to such problems.

In New York, for example, there is a large artery bank operated by the New York Society for Cardiovascular Surgery and supported by the New York Heart Association. Vessels are available at all times. Figure 10 shows one being used for a graft in a patient's femoral area. Such procedures have been performed sufficiently often to prove that they are effective.

Figure 11, which depicts the postoperative result of the procedure illustrated in Figure 10, shows an adequate graft. The graft was large, extending from the common femoral to the popliteal artery. We used the aorta of a 5-year-old child, and pieced 5 sections together in order to obtain sufficient length to bridge the gap. However, some of these grafts are not satisfactory.

The problem with the prosthetic devices has been mechanical. It has been necessary to obtain a substance that will accept and absorb the thrust of the heartbeat.

When grafting is considered, the important problem in each case is whether there is an adequate distal vessel to carry the blood away. If there is not such a distal vessel, a graft will fail and may make the patient's condition even worse.

FIG. 9. Vessels of popliteal space, showing insufficient collateral circulation. (Reproduced with permission from Pratt, G. H.: Cardiovascular Surgery. Philadelphia, Lea & Febiger, 1954.)

Figure 12 is an aortogram showing an obstruction in the iliac artery. At operation it was found to be nearly complete, with only a small amount of blood flowing through it. We replaced the obstructed area with a nylon-type graft.

One type of graft now available has an accordion-like section, which enables it to expand with the blood flow. The future of all such grafting probably lies in prosthetic devices.

It is wise to remember that these procedures exist and that some patients, even elderly ones, can be given at least a chance at repair.

Although repair is impossible in some patients, the defect can be obliterated (Fig. 13). This type of therapy, which was used by Dr. Matas over fifty years ago, is still good when replacement is technically impossible.

FIG. 10. Vessel from artery bank being used for a graft in the femoral area. (Reproduced with permission from Pratt, G. H.: Cardiovascular Surgery. Philadelphia, Lea & Febiger, 1954.)

FIG. 11. Postoperative result of the procedure illustrated in Figure 10, showing an adequate graft. (Reproduced with permission from Pratt, G. H.: Cardiovascular Surgery. Philadelphia, Lea & Febiger, 1954.)

MODERATOR STONE: Dr. Paul, you have a question from the audience. Will you read and answer it?

DR. PAUL: *What are the diagnostic criteria of beriberi heart disease in geriatric patients with nutritional deficiency?*

FIG. 12. Aortogram showing obstruction in the iliac artery, which was found at operation to be nearly complete. The obstructed area was replaced with a nylon graft.

FIG. 13. Showing obliteration of arterial defect.

Most of these patients are either alcoholics or some type of food faddist. In geriatric practice, patients may be observed who are so specific in their food habits that their diet becomes deficient.

The pertinent findings include a rapid pulse, widening of the pulse pressure, warm skin, elevation of the venous pressure (as shown by distension of the neck veins), and enlargement of the heart (as shown by roentgenograms).

These patients usually have other signs of associated vitamin deficiency. They do *not* show classic evidence of the more common varieties of heart disease; they do not have typical angina, hypertension, nor signs of organic disease of the valves, although they may have associated systolic murmurs due to cardiac dilatation. Their circulation times are normal, or even less than normal. These patients respond, not to digitalis or the standard measures used in the treatment of congestive heart failure, but to proper diet, particularly to large doses of thiamine chloride.

MODERATOR STONE: Do you find evidence of protein deficiency in these patients?

DR. PAUL: Yes, because associated deficiencies are common. Rare indeed is the patient whose only deficiency is that of thiamine.

MODERATOR STONE: Dr. Griffith has a question.

DR. GRIFFITH: *What is your experience in using stellate-ganglion block in the treatment of cerebral arteriosclerosis?*

We do not use a block for the treatment of cerebral arteriosclerosis. In the past, we used it frequently in patients with cerebrovascular accidents when we were positive no hemorrhage had occurred even though cerebral thrombosis or embolism might be present.

Experience in the neurosurgical and the medical departments of our hospital has been as follows: If too much time is taken in assembling the equipment and performing the blocks, evidences of injury in the patient probably have disappeared or are rapidly disappearing. If, after half an hour or an hour, we perform the block in a person who has not recovered spontaneously, we do him no good. Therefore, we have stopped using stellate-ganglion blocks for the treatment of cerebral thrombosis and embolism.

MODERATOR STONE: Our experience has been similar.

We should like to discuss some other topics, namely, the shoulder-hand syndrome and the indications and contraindications for the use of anticoagulants, but time will not permit.

I cannot, however, close this panel without introducing one other item for brief discussion: the use of digitalis for patients in whom congestive heart failure develops following myocardial infarction.

Dr. Paul, have you something to say on that?

DR. PAUL: Digitalis is not indicated as a routine measure in patients with myocardial infarction. However, if congestive heart failure is present, it is reasonable and proper to give digitalis to these patients.

The ill repute that digitalis has acquired in this instance probably is largely

due to the fact that patients with myocardial infarction and congestive failure have a lower survival rate and a higher mortality rate in any event.

In my opinion, the indication for the use of digitalis in patients with myocardial infarction is the presence of definite signs of congestive heart failure.

DR. GRIFFITH: I agree. Digitalis therapy should be started as soon as the physician is certain that congestive failure is present.

MODERATOR STONE: When you do start digitalis, you anticipate, of course, that it may cause some disturbance in rhythm. Do you use any methods specifically intended to protect the patient from such disturbance?

DR. PAUL: The best preventative is adequate oxygenation of the myocardium. I do not recommend that the patient receiving digitalis for congestive heart failure with myocardial infarction be given any treatment specifically designed to prevent arrhythmia. He should be kept compensated and oxygenated. If arrhythmia develops, the medication can be stopped.

When the serum potassium level is low, the patient may benefit from the administration of potassium if arrhythmia develops. The use of a drug such as procaine amide might be indicated.

DR. GRIFFITH: I agree.

MODERATOR STONE: I wish to thank the collaborators who have made this panel possible.

CONNECTIVE TISSUE, HORMONES AND AGING

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A conception of the biology of the aging process is of importance in the clinical management of elderly patients. The study of collagen diseases has directed attention to the anatomy and physiology of connective tissue (1). The biochemistry of an amorphous component, ground substance, involves functions of the entire organism. The diminishing amount of ground substance with increasing age (2) may be correlated with characteristic physiologic reactions of senility. As far back as 1800 Xavier Bichat, a French physiologist, pointed out that the connective tissue is an organ (3). Today it is conceived as an organ of defense and nutrition, as well as support for the body (4). The bones, joints and ligaments clearly demonstrate the support function. In tissue repair, the fibroblast function is most prominent, but clasmatocytes, mast cells and plasma cells are also involved. The plasma cell produces gamma globulin (5), a blood factor which protects against infectious disease.

CONNECTIVE TISSUE

The connective tissue is made up of three types of fibers (collagen, reticular and elastic) and the amorphous ground substance (6). This is the intercellular substance and occurs as a hydrated gel. It transmits water, electrolytes, vitamins, hormones, and protein products between the vascular space and the intracellular space. The cement substance between the cells of the capillary wall is composed of ground substance. The reticular fiber with ground substance forms the basement membrane of parenchymatous tissue and provides the supporting structure. The collagen fiber is built up by an interaction between the fibroblast and the ground substance. Vitamin C is necessary in this process (7), and the practice in surgery of using large doses of this vitamin in the elderly helps prevent wound dehiscence. The elastic fibers are not manufactured again in the body after embryonic life.

Ground substance is abundant in the infant, less plentiful in the adult, and scanty in the elderly. Its abundance in the infant increases the size of the interstitial space. In the adult the varying interstitial space averages about 11 per cent of the body weight, whereas the vascular space is 5 per cent and the intracellular space is 40 per cent. In the infant, however, the interstitial space may be 30 to 40 per cent of the body weight. To correct fluid balance in the infant, one must calculate with a different formula. The scantiness of ground substance in the elderly, as well as the diminished lean muscle mass may be correlated with a vulnerability to shock. The concept of "chronic shock" indicates the tendency of the elderly and debilitated to go into a state of shock under a major stress (8). Diminution of the ground substance results in a smaller reserve

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area to meet changes in vascular volume. This relation of vascular volume to lean muscle mass and diminished ground substance makes it difficult to correct the rapid changes which occur in disease, injury and surgery.

The amount of ground substance in the umbilical cord (Wharton's jelly) is large. When the umbilical cord is formed in the embryo, such an amount of gelatinous extracellular substance is characteristic of the embryo as a whole. Starting with the fertilized ovum, a growing sheet of cells becomes a sphere which dents inward, forming an inner layer (entoderm) and an outer layer (ectoderm). Between the cells and between the two layers is formed a large amount of amorphous intercellular substance. This stage of the embryo is comparable to the coelenterate in biology, so that the umbilical cord forming at this time may have a jellyfish appearance. If intercellular substance becomes scanty in senescence, is it closely related to the basic process of senescence?

Changes in the cell after its peak of activity are signs of natural decline. Aging of the whole person is not the same as decline of the component parts. Aging of tissue appears even before birth, and the placenta is senescent by the time of birth, showing fibrosis and even calcification (9). The ductus arteriosus, which shunts the blood past the lungs before birth, exhibits soon after birth an arteriosclerotic process comparable to that in the arteries of an old man. Nerve endings sensitive to changes in oxygen tension of the blood after opening of the lungs plus an abundance of elastic fibers in the ductus keep it closed off after birth and defunctionate it.

Cell division characterizes young tissue; and when mitosis ceases, aging has begun. However, the life history of the organism indicates that some growth processes must be arrested at maturity for survival of the species. Birth is a climactic event in which a parasite which has been drawing sustenance through an umbilical cord changes to a physically independent being which inspires its own air and digests its own food. The onset of physiologic maturity of the individual is less spectacular; it coincides with a period of reproductive capacity. Cellular changes and the slow-down of growth suggest aging. Progression of such changes becomes senile degeneration. Maintenance of health and the inhibition of the aging potential are the main factors in the problem of control of senescence.

Sexual reproduction is a biologic method for rejuvenation of the protoplasm of the higher forms of life. This device occurs in certain plants (algae) only under the stress of adverse conditions which would cause aging of the cell. In mammals, aging may affect all the body cells (including germplasm). Among rotifers, the offspring of older parents usually manifest senescence earlier in life, reflecting the increased aging potential of the tissues of the parents (10).

Since "aging" of some cells and maturing of the individual produces the adult, it is seen that for development of the organism the *loss of integrity of some cells by aging may be necessary*. In the eye of the fetus, cells of the anterior epithelium of the lens lose their nuclei and become drawn out to form lens fibers in which the cytoplasm becomes very refractive. The loss of such cells produces the specialized organs. It is the timing of these anatomic sacrifices that constitutes

the orderly development of the individual. If such timing is upset, as by a premature birth, and the premature newborn infant is overstimulated with oxygen (11), the disturbance in connective-tissue function may result in retrolental fibroplasia and blindness. With the skin, it is only through the death of some of the outer epidermal cells that we have this efficient outer coating. The basal layer of the epithelium produces cells that become transformed to the protective stratum corneum. This forms the intersurface between the primordial sea water of our tissue fluids and the atmosphere in which we live. Although aging of some cells is necessary for protection, the problem is to recognize the nature of senescence and to retard the process of degeneration. Cells vary in behavior and we must determine what causes degenerative changes in individual cells. Whereas the basal cells of the skin reproduce readily, the mature nerve cells and the polymorphonuclear leukocytes are not capable of reproduction. In the liver, the cells are in constant renewal; in other tissues the power of reproduction has become reduced. Evidence of aging, as in the nerve cell, is furnished by accumulations of lipoid (12) and pigment granules (13). As an ultimate event of aging, cytolysis (self-destruction) is seen in the sebaceous gland. This transformation of the cell body forms the gland secretion. In the leukocyte, cytolysis is seen as a process which releases enzymes to destroy the invader and erode the host tissues to drain the suppurative process. Whereas some living cells approaching death seem to provide for their own liquefaction, the aging process in cartilage is characterized by calcification. The brittleness of aging bone is associated with a loss of elasticity and senile osteoporosis. With aging, there is an alteration of the metabolic turnover in connective tissue.

The *calcium ion* is important in the interstitial space. All the calcium in ground substance (500 mg. in the adult) is ionic (14), and the total amount present in the ground substance of the body may pass out of it within one minute. In the blood stream, half of the calcium (a total of 280 mg. in the adult) is in ionized form, the remainder is in the form of molecules in solution. The soluble salts are diffusible and can pass from the intestinal tract to the blood stream and to the kidneys. The ready source of metabolic calcium is the massive storage area of the bones. Studies with liver cells show that in young animals the calcium turnover is rapid and the calcium uptake of the cells is low (15); in old animals the reverse is true and the cells take up more calcium. Aging, therefore, is correlated with a sluggish calcium metabolism. As the potassium-ion function predominates in the intracellular space, so the calcium-ion function predominates in the interstitial space. Interstitial calcification is associated with senile degeneration, and the secret of aging may be part of the total story of calcium metabolism.

Calcium turnover is through the ground substance. The mucopolysaccharides of ground substance are chondroitin sulfate, hyaluronic acid, and at least three others (16). Mucopolysaccharides lend themselves to the process of calcium turnover, and pathologic calcium deposition occurs when the ground substance is destroyed. Chondroitin sulfate excreted into the urine exerts a "protective colloid" action to keep the calcium molecules in dispersion and prevent formation of calculi. Chondroitin sulfate added to a suspension of calcium salt delays

sedimentation. Osteoporosis, which is characteristic both of old age and of disuse atrophy, involves loss of calcium from bone after the cessation of muscular activity. This process is quite striking in paraplegics, in whom copious excretion of calcium from the bone leads to bladder calculi.

STRESS

That inactivity is detrimental to homeostasis has been proved frequently in clinical experience. Early postoperative ambulation is standard today and reduces the probability of thrombo-embolic disease. Although the danger of immobilization for the elderly has been well known, the advice for greater muscular activity in heart disease has lately become routine. Medical experience among prisoners of war has shown how lethal inactivity can be. When starvation, malaria and dysentery prevailed, observation showed that men who lay in their bunks died, and that those who kept moving about survived. Men seemed to die because they "gave up," and the term for this condition ("bambooitis") referred to the recumbent position on the bamboo sleeping platforms.

The negative nitrogen balance of enforced immobilization showed up in a group of diphtheria cases. A prison-camp epidemic left many with toxic myocarditis. Absolute rest for heart disease was current practice at that time. However, the refractory patients who disobeyed the order to lie still, seemed to have a lower mortality rate. The higher incidence of diabetes, duodenal ulcer, and coronary heart disease among nonactive workers has led to the designation of "hypokinetic disease" for these entities (17). Selye has included these in his concept of adaptation syndrome, which involves an untoward balance of adrenocortical secretion.

A London bus company's experience with heart disease showed that among conductors who run up and down between the two decks there was a lower rate of heart attacks than among the drivers who remain seated on duty. It may be that tenseness, overstimulation, and physical inactivity create severer stresses than muscular activity; the tense alertness required of the driver is not required of the conductor. The avoidance of stresses that lead to senescence depends on the maintenance of a dynamic balance of body functions. Absence of stimulation is deadly, just as is overstimulation. Chilling and exposure are undesirable, but so are overheated houses. Either starvation or overeating is detrimental.

Avoiding stress requires a measure of moderation. Yet, there is a wide range in "moderation." In rehabilitation, it takes resistance exercises to restore muscular strength to atrophied structures. The longevity of George Washington is attributed by a physician-writer to the constant stimulation of his hormones by the stresses of his responsibilities (18). Life cannot be devoid of stress, but one must plan to avoid needless or prolonged stress.

HORMONES

Just what may best protect the blood vessels from degeneration is not certain. Atherosclerosis may be caused by a disorder of fat metabolism involving lipoproteins, cholesterol and fat. Anoxia in kidney tissue produces a VEM (vaso-

excitor material) hormone which causes vasoconstriction and hypertension, and can aggravate existing damage in cerebral blood vessels. There is experimental evidence (19) for another factor—desoxycorticosterone acetate (DCA) plus salt has an increased atherogenic effect if one kidney of the experimental animal is removed. DCA stimulates proliferation of fibroblasts and increases osmosis, whereas cortisone inhibits experimental wound healing and suppresses osmosis. Testosterone is found to stimulate production of ground substance (20, 21), and the same is true of estrogen (22). Oral intake of androgen and estrogen as a dietary supplement for the elderly has become common clinical practice (23). The fact that women outlive men suggests that the action of estrogenic hormone during maturity is more contributory to inhibiting degenerative aging than is androgen. However, such an advantage could not be gained in the male without feminization. Maintenance of hormone balance, the internal climate of the body, may require destruction of excesses as well as substitution therapy in hormone deficiency. Hormones influence the enzyme systems which control the metabolic consumption of minerals and nutrients. Whereas in the early embryo all the cells produce a gelatinous intercellular substance, in the adult the production of ground substance is carried on only by the fibroblast. If androgen-estrogen hormones inhibit senile decay, the suggestion follows that the individual no longer capable of reproduction is of no use to Nature for species survival.

Ovarian secretion enters into the metabolism for homeostasis in the female, and the female hormone pattern may be more conducive to prolonged survival than that of the male. It is probable that the life span of the male is shorter, not because his external environment is more demanding but because of his internal environment. The androgen of the adrenal fortified by the androgens of the male gonad results in sharper upsurges of energy and greater wear and tear than in the female. As a result, peptic ulcer and coronary thrombosis are more common in the male. Senescence apparently begins when sex hormones are reduced below a critical level; perhaps extinction of the gonadal hormones at about age 65 may usher in senescence.

SUMMARY

The ground substance of connective tissue functions between the living cell and its blood supply and is the important site of calcium metabolism. Ground substance is consumed in physiologic function and renewed by means of production by the fibroblastic cells. Diminished turnover of calcium and increased deposition of calcium characterizes aging tissue. Whereas ground substance is copious in the embryo and infant, it is diminished in the mature individual. Fibroblast function is affected by vitamin C. Ground substance activity is affected by the steroid hormones—desoxycorticosterone and cortisone having opposite actions. Hormones may affect the fibroblast production of ground substance. The influence of sex hormones on connective tissue may be of importance in the process of aging.

The results of overstimulation or insufficient physical activity in relation to

connective tissue function and health are discussed, as either may be a stress. The complex dynamic balances of physiologic function of the entire organism are maintained through the connective tissue, which serves for interchanges as well as support. Knowledge of this physiologic process is essential in order to understand the processes of aging. The correlation of fibroblast dysfunction with underactivity or overstimulation may add to the understanding of diseases of degeneration. Arrest of tissue growth is necessary for achievement of maturity; such tissue alterations, which resemble aging but are part of organic development, must be evaluated. Knowledge of the physiologic limitations of stress as related to function is an essential factor in determining what constitutes maximum obtainable longevity.

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MANAGEMENT OF FEAR OF DEATH IN CHRONIC DISEASE

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Shakespeare divided the life-span into seven ages. If Shakespeare were alive today he might, in view of great medical advances, add an eighth—chronic disease.

The chronically ill patient is greatly concerned over his continued impairment of function. Enabling him to use the resources he has, so that he can achieve as great a sense of physical and mental well-being as possible, should be the principal goal of treatment. However, attention only to the individual functions and the external environment without consideration of the internal environment—the patient's emotional life—will often prevent progress despite the best physical attempts at care and modification of inimical social factors.

Fear of death is ever present in the chronically ill patient in whom a fatal outcome is possible. Denying this fear by repression may render it completely unconscious; yet it can greatly influence the functioning of the body. Sometimes this influence is much to the patient's advantage, as in the case of a woman of 78 with cardiovascular-renal disease. She was so busy getting a college degree that her only "trouble" was with introductory nuclear physics. She achieved considerable publicity when she was refused admittance to a sorority rushing party to which she had received an invitation, but so stoutly maintained her right to be admitted that she finally got in. In this case, mental and physical activity were the best treatment for the patient. However, when denial of the fear of death leads to excessive activity or resistance to therapeutic procedures, it presents one of the most stubborn problems in the management of chronic disease.

Often this fear is denied by displacement to a minor concurrent ailment or to a minor aspect of a serious ailment. For example, despite serious impairment of locomotion because of cardiac disease, the patient may display great preoccupation over the relatively slight discomfort caused by bunions. Proper management of these patients demands the physician's recognition that emphasis on a minor symptom may be another manifestation of the denial of impending death.

In acute situations, in which events take place quickly, the patient's fear of death is not usually a problem for the experienced clinician. Pfister (1) has recounted thoughts of persons threatened with seemingly inescapable death. The person usually thinks of life situations in early childhood in which dangers were overcome. In the same way, the physician handling a case of acute illness becomes the magical, omnipotent figure who has come to the rescue. Under the great emotional stress, the patient lets fantasy take over logical and discriminating thought. He accepts relief of pain as relief from danger, and the calmness of the physician as proof of ultimate victory over the threat of death.

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In chronic situations, fear does not acutely overwhelm the intellect, but it may create problems which can be severely taxing to everyone concerned with the patient's care. There are valid reasons why the patient should fear the possibility and imminence of death, and in many cases a priest, minister or rabbi may prepare him for this eventuality. For others, however, either because of lack of religious belief or because of more complicated emotional problems, help by the physician is indispensable.

If the patient is successfully denying the fear of death and not hurting himself in the process, I believe it is the duty of the physician not to interfere in this "successful adaptation," even though it may involve him in half-truths. For example, a patient who previously lived alone but now is bedridden says that she has a nurse at home "for companionship," not essential medical care.

The dying patient must be treated with sympathy and consideration as a person who is undergoing grave mental and physical suffering, if such is the case. In this situation, the physician must decide if denial of the possibility of death is desirable for the patient's peace of mind. This deception is often complicated by evidences of grief and despair by close relatives, which can be very disturbing to the patient. I feel that the question of a will and other business arrangements should not be raised or persisted in if a patient in full possesssion of his mental faculties ignores it. Every person has the right to an exodus as free from suffering as possible. If a previously conscientious person who knows he is seriously ill does not put his affairs in order, this atypical behavior derives from his urgent need to obtain relief from the overwhelming fear of imminent death.

When the physician deems it opportune, some kindness on his part, such as a small gift to the patient or a casual remark focusing his attention on some event of interest to him several months hence, will do much to lift his spirits. I wish to emphasize that this personal physician-patient relationship is a very desirable feature in clinical treatment. However, this relationship, like the "transference" feelings which are revealed in the fantasies of patients undergoing psychoanalysis, must be used only in the patient's interest. The physician must respect the patient's concepts of death and religion and he must permit nothing to shatter the patient's belief in his own immortality. It is his duty to construct a frame of reference that will best serve his patient.

The degree of emotional support that patients demand from their physicians varies immensely, but some support must be regarded as essential in all disease in which death is or can become imminent. The physician must be able to understand and sympathize with the patient's religious and ethical beliefs. Therefore, he requires a tolerance of religious and ethical beliefs that are different from his own, and a personal philosophy that will enable him to maintain Osler's ideal of "Aequanimitas" (2). For clinicians whose personal beliefs and philosophy do not contain a "hereafter," I offer an approach which may help them in the management of patients with strong religious beliefs as well those searching for a belief.

Few of us ever forget the emotional impact of the first death we encounter in a patient under our care. The only certain fact about death is that it is an ab-

solute mystery. It must be faced as an unknown and approached the way one has solved other new, unknown situations in life. Psychoanalysts who dissect this fear in all its pathologic forms, especially phobic fears of disease and death, find that fear of death usually occurs in patients who feel themselves to be uniquely inadequate and unlovable. This distorted self-image is very deeply buried. Usually it results from a relationship in early life in which the parental security figure did not allow the person to feel effective, adequate and lovable. If one has an inner feeling of adequacy and can accept his imperfections, he can readily build up a record of accomplishment in childhood and adolescence so that by the time he is independent he can face completely new situations alone without undue anxiety. In my work with the emotional problems of the aged I have found, as did Sperling (3), that fear of death is a product of a disturbed love-object relationship. When a person feels lovable and adequate, this fear does not occur as an emotional problem.

A patient in whom a lump in the breast developed during psychoanalysis was told that a specimen would have to be taken for biopsy, and that amputation of the breast might be necessary. She became panicky, especially since the biopsy findings indicated malignancy, and an amputation was performed. After she returned to resume her analysis with me, she had a dream in which she relived an unhappy love affair which had occurred some twenty years before. This time the lover treated her kindly and introduced her to his mother as his fiancée. This was in marked contrast to his actual behavior. The blow to this woman's pride and her feeling of being unlovable had to be undone before she could face the new situation of death equably.

Many persons do not have this adequate image of themselves, yet function by means of "parentification" of others such as wives or husbands, relatives or business partners. Only when this prop is removed do their neurotic anxieties become manifest. A retired 70-year-old patient, alert and spry, with a severe phobic fear of death, was in good health except for a mild, symptomless hypertension. Although very successful in business, he gave all the credit to the deceased president of the company. In a dream he laid bare the image of himself and the core of his problem. "We were having a party at our house—a lot of people were there. I was sent out to get something at the store. When I came back I found that my older brother and all the men had gone, and my wife was playing cards with the women guests. I felt very lonely and went to the movies by myself." In his free associations to his fear of death, he always described it as "leaving all those who are near and dear to me."

During this patient's lifetime he had always had difficulty in forming new friendships apart from business because he felt no one but those in his immediate family could love him. When I was able to persuade him to return to full-time business activity, his fear of death subsided as new interests made him feel adequate and lovable.

News of the death of friends or relatives has a particularly disturbing effect on most patients, especially those faced with possible death. This reaction should be particularly watched for in cases that show a puzzling recrudescence or the

development of new symptoms. Often the patient cannot express the grief he really feels because it focuses his own danger too sharply.

A patient with severe arthritis, who had lived in a home for the aged for seven years, was referred to me by her physician because for two months she had had dyspepsia which he felt to be emotional in origin. The patient said that she did not like the "style of cooking"—that it disagreed with her. When asked why she had not complained previously, she said that Mrs. V., her best friend, used to cook things in her room and give them to her. Investigation revealed that she had been very dependent emotionally on Mrs. V., who had died shortly before the onset of the dyspepsia. When I saw the patient several weeks later, she wondered why I had sent for her. By then she had found a new friend, formed the same dependent attachment and felt lovable. She ate in the same dining-room food, with no extra tidbits, but remained free of dyspepsia.

The treatment, when this greatest of all fears becomes uncontrollable and breaks through the defense of avoidance and denial, is to use whatever means possible to give the patient the feeling of lovability. To use a religious term, he should be made to feel "in grace." With some patients, the physician can do so only when he assumes the role of a parent-substitute and by his attitude assures them that they are adequate and lovable. Then they can face the future secure in the knowledge that his loving care will protect them. This is the ideal relationship at the actual time of death. For some patients this attitude is very important as long as death is imminent, and one cannot do justice to them unless one attempts to minister to this need. If the physician finds he cannot help the patient who needs this reassurance, he should seek a psychiatric consultation for guidance.

When pain is a factor, with a considerable element of anxiety, the physician's reassuring attitude will often prove more effective than quick recourse to opiates. Hypodermic injections are symbolic to many patients of "the end" and thus greatly increase their fear. Opiates lower the pain threshold and set up a vicious cycle only too well known to the experienced clinician, who often does not comprehend the patient's anxiety. Eventually, opiates are given mainly for anxiety, and the pain factor is minimal.

Patients who are emotionally healthy usually can face the possibility of death calmly and carry out their responsibilities. But occasionally they, too, become disturbed because of overwhelming fear. In such cases, when the fear is more or less openly expressed, an honest discussion of death as a completely unknown experience which one can face with confidence may help to restore equilibrium, because the core of the anxiety is in the patient's guilty fears about himself. By word or attitude the physician conveys the feeling to the patient that he can handle future situations as competently and adequately as he has handled other situations in the past.

Thus, in treating the chronically ill patient who lives with the fear of death, the physician must serve as friend and counselor in order to alleviate the mental (or emotional) as well as the physical suffering.

SUMMARY

The importance of recognizing and managing the fear of death in patients with chronic disease and those who are dying has been indicated. The patient should always be encouraged to use his remaining resources. Basic principles for helping him to face an unknown future with the least anxiety are outlined. The physician should be tolerant of the patient's concept of death, and work within the framework of that ethical system to be either a magical, protecting, parental figure or a good, kind, sympathetic friend and counselor.

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SENILE MACULAR DEGENERATION: WHAT IS ITS SIGNIFICANCE?

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An ophthalmologist's report states that the patient has senile macular degeneration. What is its significance? The vision may be 6/6 in a beginning case, or may be so poor that only finger-counting ability remains.

To understand the significance of this disorder, we must know the special function of the macula. The macula is that part of the retina in which the cones are most concentrated, and consequently it is the portion of the retina having the most acute vision. The ability to read the print on this page is due to the fact that the reader's macula is functioning adequately. The macula is a very small structure, and the portion of the outside world seen by the macula is distinctly limited. If we place a dime upon this print and look directly at the dime, it is practically impossible to read any print on either side of it, unless we shift our gaze to one side of the dime. This explains why the first symptom complained of by the patient is that he has difficulty in reading. Also, distant vision in a straight line ahead (the point at which one gazes in the distance) is blurry, but it is noted that the surrounding area (called the peripheral vision) is not affected. This is why the visual acuity as tested on an eye-chart may be very poor, yet the patient can walk around with little difficulty, and can enjoy watching a large-screen television if seated far enough away.

Macular degeneration can occur at any age, but it is essentially a disease of older persons. Usually it is insidious in onset and progresses slowly. Macular degeneration occurring in older persons in whom no causative disease process can be discovered, is termed senile macular degeneration. According to Duke-Elder (1) it is due to sclerosis and obliteration of the choriocapillaris in the central area. Fortunately, senile macular degeneration tends to be self-limited, and even though the degenerative process may extend past the macula, it rarely extends sufficiently into the periphery of the retina to produce complete blindness. When this does occur, it is no longer merely macular degeneration.

Total blindness results so rarely that the patient with uncomplicated senile macular degeneration should be told that there is little chance of his becoming blind. In my own practice, the definite statement is made to the patient that he is not going blind. To a person who has lost his reading vision and who has worried over the thought of approaching blindness, it means everything to be told that he will not become blind, and that he will retain his ability to walk around. I have seen no case of uncomplicated senile macular degeneration in which the patient became totally blind—and if such a case of total blindness ever should occur, the patient will not have been harmed by my statement. I shall know that it has done my patient much good. This refers only to uncom-

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plicated senile macular degeneration. If the patient has an accompanying rapidly developing cataract, glaucoma, macular hemorrhage, or vascular disease of the retina, such a statement cannot be made.

The treatment of macular degeneration is empirical and consists of the use of vitamins, vasodilators, potassium iodide, topical dionine, intramuscular pancreatic extract, injections of crude liver, microwave diathermy to the macula, and other systemic therapy. Some ophthalomologists claim they have stayed the progress of the disease by treatment. Even though there is little proof that any specific therapy helps, general supportive measures are certainly indicated. A negative approach can be of no value to the patient.

SUMMARY

1. In senile macular degeneration, loss of vision mainly concerns close work for which sharp visual acuity is required. Vision for walking around is much less impaired, and the blurriness of distant vision is not as disabling as the loss of distant visual acuity would indicate.

2. The disease tends to be self-limiting when uncomplicated, and total blindness rarely occurs. The patients should be given that assurance.

3. Although the treatment is empirical, a negative approach to therapy is unwise.

REFERENCE

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Abstracts of Current Literature

TRATTAMENTO DELLA INSUFFICIENZA CARDIO-CIRCULATORIA CON UN NUOVO PREPARATO DI DIGITALIS PURPUREA (TREATMENT OF CARDIAC CIRCULATORY INSUFFICIENCY WITH A NEW PREPARATION OF DIGITALIS PURPUREA).

Barbano, G., and Turbiglio, P. C. *Minerva med.* **47**:II: 796, 1956; through Ciba Literature Review **2:** 7 (Jan.) 1957.

Cristafolin was used in the treatment of 65 patients suffering from heart disease with decompensation. Thirty-five of these patients also had mitral defects. Treatment was initiated with oral or rectal doses of 0.5 to 1 mg. daily, but daily dosages of 0.5 to 0.75 mg. were found to be sufficient when the drug was injected intravenously. This dosage was continued for two to ten days, until the desired response was obtained. Maintenance therapy over a prolonged period (0.1 to 0.5 mg. daily or several times a week) is of great importance, and Cristafolin, being well tolerated, is ideal for this purpose. The negative chronotropic and negative dromotropic actions of Cristafolin are noticeable within a short time. In 84 per cent of the cases of sinus tachycardia—some of them severe—the heart rate was reduced to 85 or less in six days, on an average. This level was reached in five days by as many as 97 per cent of the patients with tachycardiac arrhythmia. The pulse pressure increased in 70 per cent, and the venous pressure in 84 per cent of the patients. The speed of circulation was accelerated in 90 per cent of the cases. Some improvement in electrocardiographic tracings was recorded in almost every instance. The volume of the heart (determined radiographically) diminished in 40 per cent of the patients. Anorexia or nausea seldom occurred, and when it did, the symptoms were overcome by discontinuing treatment for two or three days.

THE MANAGEMENT OF LINGUAL CANCER.

Berridge, F. E., Jr., and James, A. G. *Surg., Gynec. & Obst.* **103:** 595 (Nov.) 1956.

Lingual cancer occurs most frequently in the male and usually occurs in the fifth or sixth decade of life. Cancers of the anterior tongue are nearly exclusively squamous-cell carcinomas and located on the lateral margin. The initial symptoms—awareness of an oral mass, local tenderness, or burning pain—are attributable to the growth itself, so that early detection is possible, although 25 per cent of patients have been found to have palpable cervical nodes upon hospital admission. Cancer of the posterior third of the tongue is less frequently squamous-cell carcinoma. It can cause the same complaints and in addition otalgia, dysphagia or dysphonia. When discovered, the primary lesions are usually large, and palpable cervical lymph nodes are present in a large percentage of patients. Syphilis appears to be less of a predisposing factor in carcinoma of the tongue that it has formerly been considered. Rather, oral hygiene and smoking seem to play a decisive role in predisposition toward lingual cancer. Associated degenerative diseases are commonly found. Asymptomatic lesions are rare. The incidence of early detection can be raised by exploration of the oral cavity of all patients during physical examinations. Oral palpation is the only readily available screening method for detecting lesions in the glosso-epiglottic fossae and at the posterior base of the tongue. An immediate biopsy is indicated when a suspicious lesion is found. The evaluation of a patient with cancer of the tongue presents no unusual problems. Intraoral palpation yields an idea of the location, size, appearance, and infiltrative extent of the lesion. When nodes are palpable in the neck, an immediate aspiration biopsy of the most suspicious cervical mass is indicated. The laboratory tests are enumerated. A chest film is necessary in order to detect distant metastases or associated cardiorespiratory disease. The size, location, and type of lesion dictate the therapeutic approach.

The principal approach is surgical. Surgical management is described for each lingual site of origin: 1) small localized carcinomas of the anterior third of the tongue are removed by transecting the apex of the tongue obliquely; 2) lesions up to 3 cm. in diameter on the lateral border of the middle third of the tongue are treated by hemiglossectomy; 3) carcinomas on the dorsum of the tongue are elliptically incised and controlled thereby unless metastasis has occurred; 4) lateralized lesions of the posterior third base of the tongue are removed through an intraoral approach, but more extensive lesions of the base of the tongue require a lateral approach. When lateral pharyngotomy is required, it is combined with a radical neck resection. In case of extensive spread onto the epiglottis or extrinsic larynx, total laryngectomy with radical neck dissection and excision of the primary lesion is required. The surgical management of involved cervical nodes is also described. Postoperative maintenance is outlined. Tracheostomy is performed following a "commando" operation (extensive procedure used in advanced cancer of the tongue with mandibular involvement) or a radical neck dissection combined with pharyngotomy. The indications for radiation therapy are summarized. External irradiation therapy is unsatisfactory because of the handicaps in its use about the head and neck. Interstitial implantation of radioactive iridium is the superior procedure. A series of 102 patients with cancer of the tongue form the basis of this report. All except 4 were subjected to surgery and given interstitial irradiation or both, with an over-all operative mortality of 2.5 per cent.

AGING AND OSTEOARTHRITIS.

Bohatirchuk, F. *Canad. M. A. J.* **76:** 106 (Jan. 15) 1957.

This is a study of bone aging based upon the thesis that all bone changes in aging man are not pathologic. The bones of 500 elderly persons, 560 human skeletons, and of aging animals were examined radiographically and historadiographically, and the data analyzed. From 60 to 70 per cent of the elderly people examined complained of no bone or joint ailments, and inspection and palpation showed no obvious abnormalities. Roentgenograms of these asymptomatic persons revealed some signs that heretofore have been considered typical of degenerative osteoarthritis. However, this research led to the conclusion that some bone changes are typical of normal (physiologic) bone aging and cannot be considered as pathologic, that is, osteoarthritic. For instance, a harmonious development of bone atrophy and bone hypertrophy was found to be typical of physiologic bone aging, whereas disharmonious development of these bone processes was found to be typical of osteoarthritis. Changes seen in normal aging included calcium decrease in bone in the sixth decade. Osteoporosis became conspicuous in the seventh decade, that is, roentgen-ray absorption in bones was diminished and morphologic signs of bone atrophy appeared. The number of trabeculae diminished, compact bone was thinned, and small cavities in spongy bone appeared. The atrophic process in bone apparently takes place slowly and is an irreversible process. Hypertrophy of bone was observed roentgenographically in the bones of all persons late in the fifth decade, and sometimes earlier. Roughness and unevenness of outlines first became apparent, and exostoses and lipping in later life. The "mushroom sign" and calcifications in tendon attachments and rib cartilages were found. In contrast, pathologic signs were found in some elderly persons and the majority of them also had such symptoms as permanent pain, considerable rigidity of the spine and joints, swelling in the area of joints, or Heberden and Bouchard nodes. However, some of the elderly people in this group had no outstanding clinical symptoms despite obvious morphologic changes in bones. In so-called symptomatic persons, the following roentgenographic signs were found: more pronounced lipping than in normal aging persons, with complete fusion of neighboring lippings in some advanced cases; exostoses not only in the periphery of the epiphysis but also in the area of the joint surfaces, often with deposition of calcium salts in their periphery; normal calcifications in intervertebral discs, joint cartilages, and joint capsules, but no extensive calcification of rib cartilages. In some cases of extreme osteoporosis, the roentgen-ray absorption by bones was the same as that in surrounding soft tissues. This state is some-

times referred to as "senile osteoporosis." In such cases, an excessive decrease in the number of bone trabeculae and almost complete disappearance of compact bone simultaneously with development of large cavities in spongy bone were sometimes seen, as well as compression fractures. Historadiographic findings in bone microstructure in normal bone aging and in osteoarthritis are discussed. A chart for the differentiation between normal and pathologic changes in the radiographic examination of bone is proposed. Although the term "osteoarthritis" is used for a group of pathologic bone processes resulting in bone destruction or bone deformation, it is probable that in the near future many entities with different names will be distinguished. The differentiation of these kinds of change has a practical importance. For example, in the case of normal bone aging, physical exercise may delay the progress of bone changes. A physician, fearing complications of a nonexisting osteoarthritis, might advise complete rest and special therapy for elderly persons with no pathologic changes in their bones.

CONSIDERAZIONI CLINICHE SU UN NUOVO PRINCIPIO PER INIBIRE LA TOSSE (CLINICAL CONSIDERATIONS ON A NEW PRINCIPLE TO INHIBIT COUGH).

Cavalca, A. *Gazz. internaz. med.* **61:** 1653, 1956; through Ciba Literature Review **2:** 26 (Jan.) 1957.

Tessalon was tested in 86 patients with coughs of diverse origin. Thirty-seven patients had acute or chronic bronchitis associated with a dry irritant cough. The intravenous injection of one to four ampules daily, or the rectal administration of 100 mg. four times a day quickly yielded good results, whereas the response was not so rapid following the ingestion of Tessalon perles or liquid. Four patients suffered from coughs due to compression of the main bronchi by lymphogranulomatous masses. Two to four ampules of Tessalon daily, injected intravenously, rapidly produced a good effect. In 10 cardiac patients with congestive bronchitis, Tessalon rectally soothed the irritant cough, thus easing the strain on the heart and helping it to respond better to cardiotonic agents. In 35 asthmatic patients—some with and some without emphysema—Tessalon not only suppressed cough, but also alleviated asthmatic symptoms and improved the findings upon auscultation. This effect was presumably due to the fact that Tessalon diminishes the sensitivity of the pulmonary stretch receptors to neuroallergic stimuli. Tessalon was well tolerated and lost none of its effectiveness even when administered for a long time. *Note:* The active ingredient of Tessalon is an ester of *p*-butyl-aminobenzoic acid.

FEBRILE COURSE OF MYOCARDIAL INFARCTION.

Flaxman, N. *Am. Pract. & Digest. Treat.* **8:** 201 (Feb.) 1957.

It is sometimes overlooked that a febrile course is one of the conditions that places a patient with an acute myocardial infarction among those with a poor prognosis. Two cases of myocardial insufficiency are presented in which the patients had none of the previously listed poor-risk features but ran a febrile course that terminated fatally. At necropsy no other cause for the elevated temperature could be discovered except the acute infarctions. Other causes of persistent fever in myocardial infarction have been reported and include myocardial abscess in the infarcted area, purulent pericarditis, and subacute bacterial endocarditis arising in mural thrombi following infarction.

PEYRONIE'S DISEASE: TREATMENT BY THE LOCAL INJECTION OF METICORTELONE AND HYDROCORTISONE.

Furey, C. A. *J. Urol.* **77:** 251 (Feb.) 1957.

The injection of Meticortelone or hydrocortisone in the treatment of Peyronie's disease (penile induration) proved of value. In 5 of 12 patients so treated (41 per cent) there was fair to excellent improvement. Pain was relieved in 61 per cent of the cases but curvature in only 30 per cent. An average of 6 to 10 injections of 25 mg. of either steroid was necessary

before any significant changes could be noted and the optimal effect was reached between 15 and 20 injections. Variations in results were attributed to the degree of fibrosis present, the extent of the lesions, the presence or absence of calcium, whether or not there was involvement of the corpora cavernosa, and the skill of the operator in injecting all of the medication into the plaque. The last is an important point, as no results can be expected without injection of the steroid directly into the plaque. In general, the best results were observed in patients with a single noncalcified nodule. In responsive patients, the plaque had been present for eight months, whereas in those who failed to respond symptoms had been present for seventeen months. When chordee was found or the corpora cavernosa involved, little improvement was seen. No appreciable difference was noted between the results with Meticortelone and those with hydrocortisone. Of the former, 133 injections were made, and of the latter, 117. The results obtained with steroids were better than those obtained in other patients with the use of roentgen-ray therapy, testosterone, or surgery. The injection of steroids in Peyronie's disease is a safe and easy method of treatment which can be employed in office practice or the outpatient department of a hospital. Further investigation is required to determine its status in the treatment of this condition.

POLYESTRADIOL PHOSPHATE FOR CARCINOMA OF THE PROSTATE: A CLINICAL STUDY.

Goodhope, C. D. *J. Urol.* **77:** 312 (Feb.) 1957.

Polyestradiol phosphate (P.E.P.) is a stable, water-soluble, white powder. Its structure contains the steroid nucleus which, through phosphorylation, has formed a molecule with a weight of approximately 15,000. P.E.P. is nontoxic in large doses, 400 mg. having been given monthly to patients for twelve months without evidence of liver damage or other undesirable effect. Orally, it has no estrogenic effect. After intravenous injection, it is rapidly bound in the reticulo-endothelial system as well as protein bound, as shown by radioactive phosphorus studies. Its fate after intramuscular injection apparently is different, since the duration of its effect is approximately doubled. The substance does not pass through the kidneys and is retained in the body, probably because of the shape and size of the molecule. After hydrolysis of the substance in the body, increased amounts of estrogen can be recovered in the urine. P.E.P. was used in the treatment of 5 patients with prostatic carcinoma who had undergone orchiectomy and received 24 mg. of TACE daily for varying periods. Each received 40 mg. of P.E.P. monthly for a year. This dosage, injected intramuscularly, maintained therapeutic estrogen levels for a month. No toxic effects were noted. Two patients with extensive metastases, who initially appeared moribund, had a remission without a change in metastases; however, after a year, a clinical decline is becoming apparent. The other 3 patients obtained subjective and clinical benefits greater than those seen with previous therapy. A delay of sixty to ninety days was apparent in some of the patients before an effect could be noted. Should confirmation of the beneficial effects of P.E.P. continue in further trials, the substance should be subjected to large-scale, long-term clinical investigation.

NONSPECIFIC CORTISONE EFFECTS FROM ACTH ADMINISTRATION IN ADVANCED PROSTATIC CARCINOMA.

Hinman, F., Jr., and Smith, G. I. *J. Urol.* **77:** 305 (Feb.) 1957.

An investigation was made of the administration of ACTH to patients undergoing an exacerbation in advanced prostatic carcinoma, in order to compare its action with that of cortisone and attempt to discover whether the effect of cortisone is due to adrenal suppression (antiandrogenic effect; medical adrenalectomy) or to a direct effect of cortisone upon the patient and the neoplasm. Eight patients in a state of relapse after orchiectomy and stilbestrol administration received 80 units of ACTH daily, along with 6 Gm. of potassium

chloride to prevent potassium deficit during adrenocortical therapy. The excretions of compound F and 17-ketosteroids in the urine were measured and correlated with the clinical effect. Effects upon the lesion, upon the levels of acid and alkaline phosphatase, and upon bony metastases were evaluated by palpation, laboratory determinations, and roentgenographic examination, respectively. ACTH produced clinical improvement comparable in quality but not in duration to that after cortisone therapy, in 3 of the 8 patients. Two other patients had short periods of improvement, but 3 had no benefit. Two of the 3 patients improved, who had proof of the greatest adrenal stimulation and had a remission in spite of the concomitant rise in 17-ketosteroid excretion which would have been expected to exacerbate the disease. These results are interpreted to mean that the clinical improvement is due to the effect of the adrenal corticoids released along with androgens. This indicates that it is not adrenal suppression but the direct action of cortisone which produces the changes seen during cortisone therapy of advanced prostatic carcinoma. The effect is not simple analgesia nor is it due to euphoria. No change could be detected in the local lesion by palpation nor in the metastases by roentgenographic examination, so that it is unlikely that the effect is one of a non-sex hormone type upon the connective tissue. Rather the effect of cortisone and to a lesser degree of ACTH therapy is believed to be exerted through a shift in the hormonal environment of the tumor.

UTILITÉ DE LA RÉSERPINE CHEZ LES CARDIAQUES NON HYPERTENDUS. (THE USE OF RESERPINE IN NONHYPERTENSIVE CARDIAC PATIENTS).

Junet, R. *Méd. et hyg.* **14:** 496, 1956; through Ciba Literature Review **2:** 6 (Jan.) 1957.

The treatment of normotensive cardiac patients with reserpine is reviewed. Junet gives these patients one or two Serpasil tablets of 0.1 or 0.25 mg. three or four times daily, the total daily dosage thus varying between 0.3 and 2 mg. of Serpasil. The drug is employed primarily because of its ability to provoke bradycardia and tranquillization and to lower blood pressure in the lesser circulation. Serpasil is the drug of choice in cases of mitral stenosis, in which it frequently brings about improvement within two hours by slowing the heart rate and enabling more blood to enter the left ventricle. As resistance in the pulmonary arterioles slackens at the same time, there is a clear-cut reduction in pulmonary stasis. In this indication, as in chronic cases of pulmonary heart disease, reserpine is undoubtedly preferable to digitalis. In cases of sinus tachycardia due to various causes (sympathicotonia, Graves' disease), Serpasil can restore the heart rate to normal within a few days. Good results may also be expected when Serpasil is used to prevent attacks of paroxysmal tachycardia. Similarly, the bradycardiac and tranquillizing effect of Serpasil can be put to good use in the treatment of coronary artery disease and the postmyocardial infarction state. The improvement ascertained by clinical examination is also reflected in electrocardiographic tracings.

DIE KLINISCHE BRAUCHBARKEIT DES BALLISTOKARDIOGRAMMS (THE CLINICAL USEFULNESS OF BALLISTOCARDIOGRAMS).

Kazmeier, F., and Schild, W. *München med. Wchnschr.* **98:** 753, 1956; through Ciba Literature Review **2:** 8 (Jan.) 1957.

The ballistocardiogram, which records the movements imparted to the body by the action of the heart, allows no conclusions to be drawn as to the stroke volume and other measurements of importance with regard to the action of the heart. On the other hand, when assessed in the light of empirically known facts, the ballistocardiogram has proved useful clinically. Deterioration—increasing with age—in the heart's functional capacity frequently leads to pathologic changes in the ballistocardiogram. Such changes are found in 12 per cent of persons less than 50 years of age, but in 51 per cent of those beyond age 50. In the case of young patients, a pathologic ballistocardiogram must be regarded as serious.

If coronary artery disease is present, the ballistocardiogram taken with the patient at rest may reveal disorders several years before they are noticeable in electrocardiographic tracings. In cases of angina pectoris, when the resting electrocardiogram is normal, it is possible to show a close connection between an abnormal ballistocardiogram and a pathologic finding with the "two step test." In coronary artery disease, when the resting electrocardiogram is abnormal, the ballistocardiogram is also abnormal in 93 per cent of cases. Myocardial infarction gives rise to marked changes in the ballistocardiogram curves, even when definite signs of infarction are not—or not yet—apparent in the electrocardiogram. Whereas, in this disease, the curve usually remains abnormal for elderly subjects, it may become normal again in the case of younger patients.

TONIC EFFECTS OF NEOBON THERAPY IN GERIATRIC PATIENTS.

Klemme, H. L. *Clin. Med.* **3:** 951 (Oct.) 1956.

Neobon capsules containing a low dosage of methyltestosterone and of ethinyl estradiol in the proper ratio, digestive enzymes, glutamic acid, hematinic substances, an essential amino acid, vitamins, and minerals were administered to 35 patients between the ages of 52 and 87 years. The diagnoses in the numbers of patients stated were as follows: debility, senile and general, 23; heart disease and debility, 5; thyrotoxicosis, 1; tuberculosis, acute and arrested, 2; osteoporosis, 1; avitaminosis, 1; arthritis and nutritional deficiency, 1; and male climacteric, 1. A dosage of one to three capsules daily was administered for an average of forty days. Marked improvement with mental and physical betterment of the patient, usually within two weeks, occurred in 31 patients. A slow initial response but later good improvement occurred in 2 patients. Two others showed little or no benefit. Hypertensive patients were more easily controlled when Neobon was administered as adjunctive therapy. Neobon produced a feeling of well being in the majority of patients. They had better appetites and better flexibility of limbs, and showed improved social behavior. No undesirable side-actions occurred.

EFFECTS OF FAT INGESTION AND HEPARIN ADMINISTRATION ON SERUM LIPIDS OF "NORMAL", HYPERCHOLESTEROLEMIC, HYPERLIPEMIC AND ATHEROSCLEROTIC SUBJECTS.

Kuo, P. T.; Joyner, C. R., and Reinhold, J. G. *Am. J. M. Sc.* **232:** 613 (Dec.) 1956.

The effects of fat ingestion and heparin administration upon serum lipids were investigated in 10 normal subjects, and in 12 hypercholesterolemic, 7 hyperlipemic, and 15 atherosclerotic patients. Upon paper electrophoresis, there was a sharp increase in height and some increase in width in the serum beta-lipid zone of hypercholesterolemic patients. In patients with hyperlipemia, this lipid zone became very broad and the increase in height was less. In both groups of patients the alpha-lipid zone was consistently small. Eight of 15 atherosclerotic patients were found also to have hypercholesterolemia or hyperlipemia or both. In the 7 who had normal blood chemistry levels, the electrophoretic patterns were relatively normal. Heparin given in 10-mg. to 25-mg. doses intravenously in the fasting state caused little or no change in the serum lipid levels and electrophoretic patterns in normal and hypercholesterolemic subjects, but produced sharp changes in the hyperlipemic patients. Seven atherosclerotic patients whose serum lipid levels were normal or borderline-normal in the fasting state showed a slightly broadened beta-lipid zone and a moderate increase in electrophoretic mobility of all their serum lipid zones after heparin administration. A varying but progressive increase in the width of the beta-lipid zone was observed in all subjects during the postprandial period. Heparin given during the postprandial hyperlipemic state caused a marked increase in the electrophoretic mobility of both the alpha-lipid and beta-lipid zones in all subjects. The alpha zone moved ahead of serum albumin, and the beta zone migrated with the speed of alpha lipoproteins. No evidence was found to indicate that

heparin can cause a transformation of the beta lipoproteins to alpha lipoproteins. No significant increase of heparin-like effect was demonstrable by the electrophoretic method in blood that had undergone "physiologic clearing" several hours after ingestion of a fatty meal. (From authors' summary.)

HYPERCALCEMIA IN NEOPLASTIC DISEASE.

Laird Myers, W. P. *Cancer* **9:** 1135 (Nov.–Dec.) 1956.

Data on 61 cases of hypercalcemia are presented. Fifty-three were associated with tumors, the most frequent being those of breast, lung, and kidney origin plus multiple myeloma and the lymphomas. Six patients had no evidence of metastatic disease upon skeletal survey, and later studies in one of them suggested that hypercalcemia occurred without invasion of bone. Noncancerous causes included excess calcium and vitamin D, hyperthyroidism, and hyperparathyroidism. The fact that the serum phosphorus level is slightly higher than normal in malignant bone disease and the finding of tumor cells in the patients' marrow help to distinguish malignant and nonmalignant causes. The clinical manifestations of hypercalcemia are as follows: *nervous system*—drowsiness, lethargy, confusion, coma, muscular weakness, variable reflexes; *gastro-intestinal*—anorexia, nausea, vomiting (leading to water and electrolyte losses), constipation; *renal*—polydipsia, polyuria (with further loss of water and electrolytes), albuminuria, hyposthenuria, renal failure; *cardiac*—tachycardia (or bradycardia), rhythm disturbances, cardiac failure, shortened QT-intervals, T-wave and P-wave flattening or inversion; *miscellaneous*—potassium depletion with alkalosis. The management of hypercalcemia calls for restriction of intake to 200 mg. or less per day and promotion of output to 2 liters per day. Specific measures include the use of cortisone, nitrogen mustard, 6-diazo-5-oxo-L-norleucine (DON), and disodium ethylene-diaminetetra-acetate (EDTA). Both estrogen and androgen should be stopped. Castration is of value in correcting hypercalcemia in estrogen-dependent mammary carcinoma. In the case of single malignant osseous lesions, local radiation therapy may correct hypercalcemia by destroying the tumor and thus ending osteolysis. In the case of some operable carcinomas complicated by hypercalcemia, the latter has been corrected by removal of the tumor. Because of the synergism between the effects of calcium and of digitalis on the myocardium, patients with elevated serum calcium levels should be digitalized with fractional doses and followed with the use of serial electrocardiograms. Renal failure in hypercalcemia is treated in the usual manner. Electrolyte abnormalities may occur incident to renal failure or there may be hypopotassemia with alkalosis. This should be borne in mind when the patient must receive digitalis because the potential cardiac toxicity of a given level of serum calcium will be enhanced by hypopotassemia. Pathologic fractures can intensify hypercalcemia because the immobilization incident to their treatment may lead to osteoporosis. Cortisone, rather than a potentially marrow-depressing agent, should be used if marked myelophthisic anemia is present.

THERAPEUTISCHE VERSUCHE ZUR SYMPTOMATISCHEN BEHANDLUNG PSYCHONEUROTISCHER STÖRUNGEN (THERAPEUTIC TESTS IN THE SYMPTOMATIC TREATMENT OF PSYCHONEUROTIC DISTURBANCES).

Miescher, P. *Praxis* **45:** 1041, 1956; through Ciba Literature Review **2:** 22 (Jan.) 1957.

Serpatonil (Serpasil and Ritalin in combination) is well suited for the symptomatic treatment of various psychoneurotic or functional disorders in which an organic lesion either cannot be found or is clearly overshadowed by the psychic component. The initial dosage was two tablets of Serpatonil in the morning, possibly followed by a third tablet at lunch time. The drug should not be given in the afternoon or evening. After two weeks, it was usually possible to reduce the daily dose to one tablet in the morning. The duration of treatment varied between two weeks and seven months. The effect of Serpatonil was generally apparent within a few days and was beneficial in 40 of the 56 patients treated.

A good response was elicited in 17 of 18 patients with tachycardia or functional heart disorders. Depressive states due to a variety of causes were positively influenced in 11 of 12 cases. The patients are now going about their affairs with greater interest and energy. Ten patients with hypertension, who complained of severe fatigue after receiving Serpasil alone, were given instead one to two tablets of Serpatonil in the morning and 0.25 to 0.5 mg. of Serpasil in the evening. The desired results were achieved in every case. On the other hand, Serpatonil proved ineffective in 11 cases of neurasthenic or arteriosclerotic hyperexcitation.

CARCINOMA OF THE ENDOMETRIUM.

Mintz, N. *J. Mt. Sinai Hosp.* **23:** 816 (Nov.–Dec.) 1956.

The literature on endometrial carcinoma and the results of treatment in 156 patients with the disease are reviewed. Prognosis in endometrial carcinoma depends upon the duration of symptoms, the grade of malignancy, the extent of the carcinoma, the type of treatment, and the general condition of the patient. The cardinal symptom is bleeding. Pain is not a reliable index as to extension beyond the uterus. Surgery is the primary means of treatment. To increase the number of cures, a more extensive operation than panhysterectomy is required. The operative procedure should include closure of the cervical os with sutures to prevent vaginal spill, ligation of the tubes to prevent seeding of fragments of carcinoma in the abdominal cavity, complete removal of both adnexae no matter how young the patient or how early the lesion, wide dissection of the parametria and removal of at least a 2-cm vaginal cuff, and, when there is a downward extension to the endocervix, a radical Wertheim procedure with bilateral pelvic lymphadenectomy. Preoperative irradiation offers no better result than that obtained with surgery alone and causes the loss of precious time by postponing the operation. Postoperative irradiation should be used whenever there is a suggestion of extra-uterine extension or when the cancer cells have a highly anaplastic appearance. The over-all five-year cure rate in the series of patients reported was 70.9 per cent, and 76.5 per cent among those treated by surgery alone.

THE PATHOGENESIS OF IDIOPATHIC HYDROCELE AND A SIMPLE OPERATIVE TECHNIQUE.

Özdilek, S. *J. Urol.* **77:** 282 (Feb.) 1957.

The vaginal sac around the testis normally contains a few drops of clear, serous fluid which increases in amount when hydrocele is present. Hydrocele probably occurs because of an imbalance between the rate of secretion and absorption of this fluid. In acute hydrocele, there is overproduction of fluid, and in chronic hydrocele impairment of reabsorption of the fluid due to insufficiency of the lymphatic system. The present methods of operation, excision and eversion, enable the fluid confined and unabsorbed in the sac to pass into the outer layers. It is then absorbed from the lymphathics of the outer layers and carried to the inguinal lymph nodes. These procedures usually lead to such complications as infection, induration or hemorrhage, and there is no need to use them because hydrocele can be cured by maintaining a permanent window in the outer wall of the sac. The procedure is described. The secreted fluid passes through the window in the outer layers of the testis and is absorbed. This window or fenestration method has been used successfully in 70 patients, with swelling of the testis as the only complication. Withdrawing half of the fluid prior to operation is advised because the testicular swelling is believed to be due to immediate decompression of the fluid.

ORAL METRAZOL THERAPY IN SENILE MENTAL CONFUSION AND PERIPHERAL VASCULAR SPASM.

Schall, E. *Clin. Med.* **3:** 859 (Sept.) 1956.

The central tonic effect of Metrazol is illustrated in the case of an elderly confused patient who underwent such a dramatic change mentally and physically that this form of

analeptic treatment was continued vigorously. This case is presented in order to encourage the use of Metrazol in elderly confused persons who may be considered beyond help and left to vegetate without an effort to ameliorate their condition or to relieve the burden they impose upon those who care for them. A 70-year-old woman with marked peripheral arteriosclerosis of fifteen years' duration and marked mental confusion and apathy received half a dram of Metrazol Liquidum two to three times daily. Very little change was noted until 2 pints of the liquid had been ingested. The primary benefit thereafter consisted of elimination of the confusional state, and increase in physical activity. Peripheral vascular spasms of the legs were ameliorated. The improvement was attributed to a general central nervous stimulation together with increased respiration and vasomotor tone, leading to a decrease in hypoxia and to improved circulation. Cortical and subcortical cerebral stimulation and enhancement of nerve-impulse transmission across the association paths of the brain probably also contributed to the improvement. Lessening of leg cramps may have been due to improved blood supply and better oxygenation of the leg muscles with resulting improved muscle function. Possibly the improved physical status diminished local irritability and raised the threshold to pain.

ELECTROCONVULSIVE THERAPY IN PATIENTS WITH STRUCTURAL DISEASE OF THE CENTRAL NERVOUS SYSTEM.

Shapiro, M. F., and Goldberg, H. H. *Am. J. M. Sc.* **233:** 186 (Feb.) 1957.

Twenty-four patients with structural diseases of the central nervous system were treated with electroconvulsive therapy because of severe affective disturbances. Fifteen benefited significantly from this treatment. The diseases and numbers of patients were as follows: intracranial neoplasms, 6; cerebrovascular accident, 6; parkinsonism and depression, 3; traumatic spinal cord disease, 2; central nervous system syphilis, 3; dystonic and dyskinetic states, 4. On the basis of the results of this study, the authors conclude that disease of the central nervous system per se, with the exception of known intracranial tumor, is not an obligatory contraindication to electroconvulsive therapy. Electroconvulsive therapy can be highly effective in resolving severe psychiatric disturbances, despite the presence of disease of the nervous system. Other than when an intracranial neoplasm is present, the use of electroconvulsive therapy does not appear to alter the neurologic picture in patients with disease of the nervous system. It is, however, contraindicated in the presence of intracranial tumors. In such patients a rapid, persistent and severe organic mental syndrome develops, and their neurologic disability is exacerbated. The rapid appearance of a severe and persistent organic mental syndrome during the course of electro-convulsive therapy, particularly in the young and middle-age patients, should raise the strong suspicion of structural disease of the brain. In particular, the possibility of silent intracranial neoplasm should be carefully considered. Electroconvulsive therapy may have a higher risk potential in patients with cerebrovascular accidents than in patients without evidence of vascular disease of the brain. Whether this higher risk potential is specifically related to cerebrovascular or to cardiovascular disease, is not known. Hemiparesis resulting from cerebrovascular accidents may lead to asymmetric seizure patterns. In the induced seizure, the paretic limbs paradoxically are elevated higher than the unaffected ones, and the body turns to the normal side.

PRELIMINARY REPORT ON THE EFFECTS OF A PLASMA LIPID MOBILIZING FACTOR IN MAN.

Steiger, W. A.; Zarafonetis, C. J. D.; Miller, G. M.; Seifter, J., and Baeder, D. H. *Am. J. M. Sc.* **232:** 605 (Dec.) 1956.

Preliminary studies of the effects in man of a plasma dialysate, which contains a naturally occurring lipid-mobilizing factor (LMF), were undertaken. A single intravenous injection of this material in 25 patients, who were maintained in a fasting state, was followed by a marked rise in the levels of plasma total cholesterol, total fatty acids, and lipid phos-

phorus. No significant change was noted in the blood glucose level, total eosinophil counts, or coagulation times. Serial electrocardiograms and the degree of angina pectoris were unaffected in a patient with coronary artery disease. Striking hyperlipemia was also induced in patients who received LMF daily for five and fourteen days. Daily determinations of the basal metabolic rate, and weekly determinations of I^{131} uptake, complete blood counts, coagulation times, and a properdin-like substance were unchanged. Two deaths which occurred during these studies were not attributed to any toxic effects of LMF. The potential significance of LMF is discussed and attention is directed to some of the areas in which future investigation of LMF may be rewarding. (From authors' summary) *Note:* LMF has now been crystallized and appears to be a heat-stable peptide (Seifter, Baeder and Ziliken, 1956).

CONTRIBUTO CLINICO ALLO STUDIO DI UN NUOVO CALMANTE DELLA TOSSE (CLINICAL CONTRIBUTION TO THE STUDY OF A NEW COUGH SEDATIVE).

Vergani, F.; Pagani, E., and Lupacchini, A. *Gazz. med. ital.* **115:** 200, 1956; through Ciba Literature Review **2:** 27 (Jan.) 1957.

Tessalon was used to relieve coughing in 90 patients. One group comprized 10 patients with chronic bronchitis; in all of these, coughing was suppressed by administering Tessalon perles (usually 3 per day). This treatment also reduced the severity of asthmatic attacks from which some of the patients suffered. The other group was composed of 80 patients with pulmonary tuberculosis, all of whom had troublesome coughs. They did not respond to the usual drugs, frequently because of habituation. Tessalon was administered initially in the form of perles (3 to 5 daily), and later by intramuscular injection of 1 ampul morning and evening. In moderately severe and severe cases, the combination of 3 perles during the day and 1 injection in the evening proved effective. As was to be expected, the results were somewhat less satisfactory in this group of patients because of the existence of more or less extensive lesions of the bronchial mucosa which failed to improve. Nevertheless, the response to Tessalon was good or excellent in 52 patients, and in no patient did the drug prove completely ineffective. Tessalon was well tolerated. No habituation was noted, even in 4 patients who received 1 injection daily for almost a year without a decrease in effect.

UEBER DIE ALDOSTERONAKTIVITÄT UND NATRIUMRETENTION BEI HERZKRANKEN UND IHRE PATHOPHYSIOLOGISCHE BEDEUTUNG (ALDOSTERONE ACTIVITY AND SODIUM RETENTION IN HEART DISEASE AND THEIR PATHOLOGIC SIGNIFICANCE).

Wolff, H. P.; Koczorek, Kh. R.; Buchborn, E., and Köhler, M. *Klin. Wchnschr.* **34:** 1105, 1956; through Ciba Literature Review **2:** 10 (Jan.) 1957.

In patients suffering from left ventricular insufficiency with decompensation, the excretion of aldosterone and sodium usually remains more or less normal. In cases of right ventricular insufficiency with decompensation and stasis in the greater circulation, however, the aldosterone concentration in the urine is always high and the sodium level low. In cardiac patients, the amounts of aldosterone and sodium excreted are in strict inverse proportion to each other. No correlation has been found between the amount of aldosterone secreted and the volume of urine passed. The highest aldosterone concentration (up to many times normal values) and the lowest sodium excretion ($\frac{1}{60}$ to $\frac{1}{200}$ of normal) are found in untreated cardiac patients with generalized edema and ascites. Compensation of the circulation and dispersal of the edema causes the aldosterone and sodium levels to return to physiologic limits. The site and extent of the edema, as well as disturbances in the catabolism of aldosterone due to liver congestion, may account for the different behavior of aldosterone in patients suffering from left and right ventricular insufficiency with decompensation. In cases of hydropic myocardial insufficiency, the regulatory systems may perhaps respond abnormally to the various stimuli, or else the regulation of aldosterone secretion may be disturbed, with the result that sodium retention, which is controlled by aldosterone secretion, eventually becomes an independent pathologic factor.

BOOKS RECEIVED

Receipt of the following books for review is hereby acknowledged. We are glad to publish complete listings of all new books received but such listing must be regarded as a sufficient return for the courtesy of the sender. Books of particular interest will be reviewed in full as time and space permit. Additional information in regard to all listed books will be gladly furnished upon request.

THE CHEMISTRY AND BIOLOGY OF PURINES. Ciba Foundation Symposium. Edited by *G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Cecilia M. O'Connor, B.Sc.* Cloth. $9.00. Pp. 327. 124 Illustrations. J. & A. Churchill Ltd., London, and Little, Brown and Company, Boston, 1957.

INTERNAL SECRETIONS OF THE PANCREAS. Ciba Foundation Colloquia on Endocrinology, Volume IX. Edited by *G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Cecilia M. O'Connor, B.Sc.* Cloth. $7.00. Pp. 291. 100 illustrations. J. & A. Churchill Ltd., London, and Little, Brown and Company, Boston, 1956.

REGULATION AND MODE OF ACTION OF THYROID HORMONES. Ciba Foundation Colloquia on Endocrinology, Volume X. Edited by *G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Elaine C. P. Millar, A.H.-W.C., A.R.I.C.* Cloth. $8.50. Pp. 311. 114 Illustrations. J. & A. Churchill Ltd., London, and Little, Brown and Company, Boston, 1957.

GUIDE TO MEDICAL WRITING. A Practical Manual for Physicians, Dentists, Nurses, Pharmacists. By *Henry A. Davidson, M.D.*, Editor, Journal of the Medical Society of New Jersey. Cloth. $5.00. Pp. 338. The Ronald Press Company, New York.

CASEWORK SERVICES FOR OLDER PEOPLE. By *Constance E. Kellam and Mrs. Johnnie U. Williams* of the Lake County (Indiana) Department of Public Welfare. Pamphlet. 50¢. Pp. 12. American Public Welfare Association, 1313 East 60th Street, Chicago 37, Illinois.

MOBILIZING RESOURCES FOR OLDER PEOPLE. Proceedings of The Federal-State Conference on Aging, Washington, D. C., June 5-6-7, 1956. Sponsored by Council of State Governments, Federal Council on Aging. Paper. 65¢. Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.

MODERN TRENDS IN GERIATRICS. Edited by *William Hobson, B.Sc., M.D., D.P.H.*, Professor of Social and Industrial Medicine, University of Sheffield. Cloth. $13.50. Pp. 422. Paul B. Hoeber, Inc., New York.

PROBLEMS OF AGING. Edited by *Robert L. Craig, M.D.* A collection of papers presented at The Annual Graduate Fortnight (October, 1955) of the New York Academy of Medicine. Paper. $3.50. Pp. 240. Distributed by George Eliot, Medical and Scientific Books, 1302 Second Avenue, New York 21, N. Y.

MODERN OFFICE GYNECOLOGY. By *George Blinick, M.D., F.A.C.S.*, Attending in Obstetrics and Gynecology, Beth Israel Hospital, New York City; Visiting Gynecologist, Harlem Hospital, New York City; Assistant Clinical Professor

of Obstetrics and Gynecology, New York University College of Medicine; Diplomate, American Board of Obstetrics and Gynecology and *Sherwin A. Kaufman, M.D., F.A.C.S.*, Associate Attending in Obstetrics and Gynecology, Beth Israel Hospital, New York City; Medical Director, Planned Parenthood of Manhattan and the Bronx, New York City; Diplomate, American Board of Obstetrics and Gynecology. Paper. $4.50. Pp. 218. 47 Illustrations. Lea & Febiger, Philadelphia, 1957.

FLEXIBLE RETIREMENT. Evolving Policies and Programs for Industry and Labor. Edited by *Geneva Mathiasen*, Executive Secretary, National Committee On The Aging of the National Social Welfare Assembly. Forewords by *G. Warfield Hobbs*, Vice President, The First National City Bank of New York and Chairman, National Committee On The Aging, and *Frank J. Sladen, M.D.*, Chairman, Committee of Trustees of McGregor Fund. Cloth. $3.75. Pp. 226. McAinsh & Co., Limited, Toronto, and G. P. Putnam's Sons, New York, 1957.

THE AMERICAN FLUORIDATION EXPERIMENT. By *F. B. Exner, M.D.*, and *G. L. Waldbott, M.D.* Edited by *James Rorty*. Cloth. $3.75. Pp. 277. The Devin-Adair Company, New York, 1957. Canadian Agents: Thomas Nelson & Sons, Ltd., Toronto.

RHEUMATIC DISEASES, RHEUMATISM AND ARTHRITIS. By *Heinrich G. Brugsch, M.D., F.A.C.P.*, Assistant Professor in Medicine, Tufts University Medical School; Physician-in-Charge, Arthritis Clinic, The Boston Dispensary; Physician-in-Chief, Rehabilitation Institute, The Boston Dispensary. Cloth. $10.00. Pp. 330. J. B. Lippincott Company, Philadelphia and Montreal, 1957. Distributed in Great Britain by Pitman Medical Publishing Co., Limited, London.

BLADDER TUMORS: A SYMPOSIUM—under auspices of American Cancer Society. Cloth. $4.00. Pp. 92. J. B. Lippincott Company, Philadelphia and Montreal, 1957. Distributed in Great Britain by Pitman Medical Publishing Co., Limited, London.

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